10/506,998

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	844	(544/242,514/256).CCLS.	US-PGPUB; USPAT	OR	OFF	2007/06/01 15:26
L2	326	l1 and inhibitor	US-PGPUB; USPAT	OR	ON	2007/06/01 15:26
L3	5	l2 and histone	US-PGPUB; USPAT	OR	ON	2007/06/01 15:27
L4	0	l3 and deacetylase	US-PGPUB; USPAT	OR	ON	2007/06/01 15:27

10/506,998 search after election

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS  1          Web Page for STN Seminar Schedule - N. America
NEWS  2  JAN 08  CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS  3  JAN 16  CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS  4  JAN 16  IPC version 2007.01 thesaurus available on STN
NEWS  5  JAN 16  WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS  6  JAN 22  CA/CAplus updated with revised CAS roles
NEWS  7  JAN 22  CA/CAplus enhanced with patent applications from India
NEWS  8  JAN 29  PHAR reloaded with new search and display fields
NEWS  9  JAN 29  CAS Registry Number crossover limit increased to 300,000 in
                 multiple databases
NEWS 10  FEB 15  PATDPASPC enhanced with Drug Approval numbers
NEWS 11  FEB 15  RUSSIAPAT enhanced with pre-1994 records
NEWS 12  FEB 23  KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13  FEB 26  MEDLINE reloaded with enhancements
NEWS 14  FEB 26  EMBASE enhanced with Clinical Trial Number field
NEWS 15  FEB 26  TOXCENTER enhanced with reloaded MEDLINE
NEWS 16  FEB 26  IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 17  FEB 26  CAS Registry Number crossover limit increased from 10,000
                 to 300,000 in multiple databases
NEWS 18  MAR 15  WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19  MAR 16  CASREACT coverage extended
NEWS 20  MAR 20  MARPAT now updated daily
NEWS 21  MAR 22  LMPI reloaded
NEWS 22  MAR 30  RDISCLOSURE reloaded with enhancements
NEWS 23  APR 02  JICST-EPLUS removed from database clusters and STN
NEWS 24  APR 30  GENBANK reloaded and enhanced with Genome Project ID field
NEWS 25  APR 30  CHEMCATS enhanced with 1.2 million new records
NEWS 26  APR 30  CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 27  APR 30  INPADOC replaced by INPADOCDB on STN
NEWS 28  MAY 01  New CAS web site launched
NEWS 29  MAY 08  CA/CAplus Indian patent publication number format defined
NEWS 30  MAY 14  RDISCLOSURE on STN Easy enhanced with new search and display
                 fields
NEWS 31  MAY 21  BIOSIS reloaded and enhanced with archival data
NEWS 32  MAY 21  TOXCENTER enhanced with BIOSIS reload
NEWS 33  MAY 21  CA/CAplus enhanced with additional kind codes for German
                 patents
NEWS 34  MAY 22  CA/CAplus enhanced with IPC reclassification in Japanese
                 patents

NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
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FILE 'HOME' ENTERED AT 15:51:20 ON 01 JUN 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 15:51:35 ON 01 JUN 2007
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STRUCTURE FILE UPDATES: 31 MAY 2007 HIGHEST RN 936320-32-0
DICTIONARY FILE UPDATES: 31 MAY 2007 HIGHEST RN 936320-32-0

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=>
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L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

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26.4% PROCESSED 2000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 146558 TO 157002
PROJECTED ANSWERS: 52906 TO 59258

L2 50 SEA SSS SAM L1

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FULL SCREEN SEARCH COMPLETED - 151121 TO ITERATE

100.0% PROCESSED 151121 ITERATIONS 55497 ANSWERS
SEARCH TIME: 00.00.02

L3 55497 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.10	172.31

FILE 'CAPLUS' ENTERED AT 15:52:20 ON 01 JUN 2007
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FILE COVERS 1907 - 1 Jun 2007 VOL 146 ISS 24
FILE LAST UPDATED: 31 May 2007 (20070531/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

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=> s l3 full
L4 14982 L3

=> s l4 and histone deacetylase
33393 HISTONE
25209 HISTONES
38650 HISTONE
(HISTONE OR HISTONES)
6959 DEACETYLASE
1672 DEACETYLASES
7341 DEACETYLASE
(DEACETYLASE OR DEACETYLASES)
5913 HISTONE DEACETYLASE
(HISTONE(W)DEACETYLASE)
L5 80 L4 AND HISTONE DEACETYLASE

=> s l5 and inhibit!
140478 INHIBIT!
L6 2 L5 AND INHIBIT!

=> d ibib abs hitstr tot

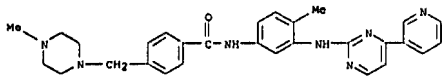
L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1133489 CAPLUS
DOCUMENT NUMBER: 146:155495
TITLE: Cytotoxic effects of histone deacetylase inhibitor FK228 (depsipeptide, formally named FR901228) in combination with conventional anti-leukemia/lymphoma agents against human leukemia/lymphoma cell lines
AUTHOR(S): Kano, Yasuhiko; Akutsu, Miyuki; Tsunoda, Saburo; Izumi, Tohru; Kobayashi, Hiroyuki; Mano, Hiroyuki; Furukawa, Yusuke
CORPORATE SOURCE: Division of Hematology, Tochigi Cancer Center, 4-9-13 Yonan, Utsunomiya, Japan
SOURCE: Investigational New Drugs (2006), Volume Date 2007, 25(1), 31-40
CODEN: INNDDX; ISSN: 0167-6997
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB FK228 is a novel antitumor depsipeptide that inhibits histone deacetylases and restores the expression of genes aberrantly suppressed in cancer cells. This agent was shown to have broad antitumor activity in preclin. studies, and is currently under phase I/II evaluations. Because of its wide spectrum of actions, it is reasonable to consider the combination with other anticancer drugs in clin. application. We studied the cytotoxic interaction of FK228 in combination with conventional antileukemic agents using human promyelocytic leukemia HL60, Philadelphia chromosome-pos. (Ph+) chronic myelogenous leukemia KU-812, T-cell lymphoblastic leukemia MOLT3 and Burkitt's lymphoma Raji cell lines. For the combination of FK228 and imatinib, Ph+ leukemia KU812, K562 and TCC-S cell lines were used. The cells were exposed simultaneously to FK228 and other agents for 4 days. Cell growth inhibition was determined by using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. We used the isobologram method of Steel and Peckham to evaluate the cytotoxic interaction at the concentration of drugs that produced 80% cell growth inhibition (IC80). FK228 showed an additive effect with cytarabine, carboplatin, doxorubicin, etoposide, 4-hydroperoxy-cyclophosphamide, 6-mercaptopurine and SN-38 (active metabolite of irinotecan) in all cell lines studied. FK228 with

methotrexate and vincristine showed an antagonistic effect in three and one of the four cell lines, resp. FK228 was additive with imatinib in all three Ph+ leukemia cells. Our findings suggest that FK228 is a promising candidate for combining with most anticancer agents except for methotrexate and vincristine, which produce suboptimal effects.

IT 152459-95-5, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FK228 showed additive effect in combination with anticancer drugs such as cytarabine, carboplatin, doxorubicin, etoposide, 4-hydroperoxy-cyclophosphamide, 6-mercaptopurine, SN-38 and imatinib in human leukemia/lymphoma cells)

RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:99470 CAPLUS
DOCUMENT NUMBER: 142:197889
TITLE: Fluoro substituted omega-carboxyaryl diphenyl urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases
INVENTOR(S): Dumas, Jacques; Boyer, Stephen; Riedl, Bernd; Wilhelm, Scott
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009961	A2	20050203	WO 2004-US23500	20040722
WO 2005009961	A3	20050331		
WO 2005009961	B1	20050602		

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

SN, TD, TG

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CA 2532865	A1	20050203	CA 2004-2532865	20040722
US 2005038080	A1	20050217	US 2004-895985	20040722
EP 1663978	A2	20060607	EP 2004-786091	20040722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004012219	A	20060822	BR 2004-12219	20040722
CN 1856469	A	20061101	CN 2004-80021091	20040722
JP 2006528196	T	20061214	JP 2006-521221	20040722
NO 2006000870	A	20060407	NO 2006-870	20060222

PRIORITY APPLN. INFO.:
US 2003-489102P P 20030723
US 2004-540326P P 20040202
WO 2004-US23500 W 20040722

OTHER SOURCE(S): CASREACT 142:197889
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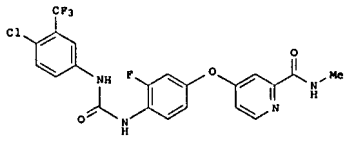

I

AB Title compound I is prepared I and salts thereof is prepared in several steps from 3-fluoro-4-nitrophenol, 4-chloro-N-methylpyridine-2-carboxamide and 4-chloro-3-(trifluoromethyl)phenylisocyanate. I inhibits PDGFR tyrosine kinase with IC50 = 83 nM. I is useful for the treatment of, e.g., inflammation and as an antiproliferative agent.

IT 220127-57-1, STI-571
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; fluoro substituted omega-carboxyaryl di-Ph urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

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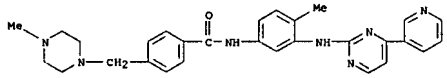
CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

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23932626 PY<2004
L7 19 L5 AND PY<2004

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L7 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1355554 CAPLUS
DOCUMENT NUMBER: 144:81158
TITLE: Use of thioredoxin measurements for diagnostics and treatments
INVENTOR(S): Marks, Paul A.; Ungerstedt, Johanna
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S. Ser. No. 369,094.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005288227	A1	20051229	US 2005-144301	20050603
US 2003235588	A1	20031225	US 2003-369094	20030214 <--
US 2006009526	A1	20060112	US 2005-223405	20050909
US 2006009527	A1	20060112	US 2005-223547	20050909

PRIORITY APPLN. INFO.:
US 2002-357383P P 20020215
US 2003-369094 A2 20030214
US 2004-577089P P 20040604

AB The invention relates to methods for monitoring patient response to histone deacetylase inhibitors (e.g., suberoylanilide hydroxamic acid (SAHA)) or other therapeutic agents by measuring the level of thioredoxin in body fluids, tissues, and/or cells, such as peripheral blood mononuclear cells, plasma, or serum. The invention also relates to methods of monitoring and/or assisting with the diagnosis of a wide variety of thioredoxin-related diseases and conditions, such as inflammatory diseases, allergic diseases, autoimmune diseases, diseases associated with oxidative stress or diseases characterized by cellular hyperproliferation.

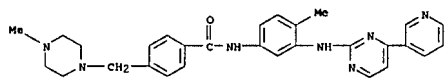
IT 220127-57-1, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(co-treatment with; use of thioredoxin expression measurements for diagnostics and monitoring treatments with histone deacetylase inhibitors and other therapeutic agents for hyperproliferative diseases)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

L7 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1004423 CAPLUS
DOCUMENT NUMBER: 143:312080
TITLE: Artificial blood vessel for delivering therapeutic agents
INVENTOR(S): Bhat, Vinayak D.; Yan, John
PATENT ASSIGNEE(S): Avantec Vascular Corp., USA
SOURCE: U.S. Pat. Appl. Publ., 52 pp., Cont.-in-part of U.S. Ser. No. 206,807.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005203612	A1	20050915	US 2003-607836	20030627
US 2002082677	A1	20020627	US 2001-782804	20010213 <--
US 7018405	B2	20060328		
US 2002114823	A1	20020822	US 2001-782927	20010213 <--

US 6471980	B2	20021029			
US 2002082679	A1	20020627	US 2001-2595	20011101	<--
US 2003083646	A1	20030501	US 2001-17500	20011214	<--
US 7077859	B2	20060718			
US 2003080692	A1	20030313	US 2002-206807	20020725	<--
US 2003017190	A1	20030123	US 2002-242334	20020911	<--
US 6858221	B2	20050222			
WO 2004010900	A1	20040205	WO 2003-US20492	20030627	
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JP 2005533604	T	20051110	JP 2004-524538	20030627	
PRIORITY APPLN. INFO.:			US 2000-258024P	P 20001222	
			US 2001-782804	A2 20010213	
			US 2001-782927	A2 20010213	
			US 2001-783253	A2 20010213	
			US 2001-783254	A2 20010213	
			US 2001-308381P	P 20010726	
			US 2001-2595	A2 20011101	
			US 2001-17500	A2 20011214	
			US 2002-347473P	P 20020110	
			US 2002-355317P	P 20020207	
			US 2002-370703P	P 20020406	
			US 2002-206807	A2 20020725	
			US 2002-404624P	P 20020819	
			US 2003-454146P	P 20030311	
			US 2003-472536P	P 20030521	
			WO 2003-US20492	W 20030627	

AB Devices and methods for reducing, inhibiting, or treating restenosis and hyperplasia after intravascular intervention are provided. In particular, the present invention provides luminal prostheses which allow for sustained or controlled release of at least one therapeutic capable agent with increased efficacy to selected locations within a patient's vasculature to reduce restenosis. An intraluminal prosthesis may comprise an expandable structure and a source adjacent the expandable structure for releasing the therapeutic capable agent into a body lumen to reduce smooth muscle cell proliferation.

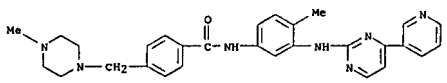
IT 220127-57-1, Imatinib mesylate 497839-62-0, AEE 788
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(artificial blood vessel for delivering therapeutic agents)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



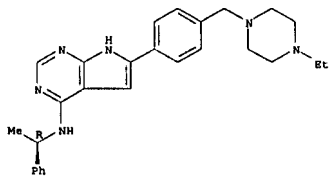
CM 2

CRN 75-75-2
CMF C H4 O3 S

RN 497839-62-0 CAPLUS

CN 7H-Pyrrolo[2,3-d]pyrimidin-4-amine, 6-[4-[(4-ethyl-1-piperazinyl)methyl]phenyl]-N-[(1R)-1-phenylethyl]- (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2003:908573 CAPLUS
DOCUMENT NUMBER:	140:192446
TITLE:	The proteasome inhibitor bortezomib interacts synergistically with histone deacetylase inhibitors to induce apoptosis in Bcr/Abl+ cells sensitive and resistant to STI571
AUTHOR(S):	Yu, Chunrong; Rahmani, Mohamed; Conrad, Daniel; Subler, Mark; Dent, Paul; Grant, Steven
CORPORATE SOURCE:	Departments of Medicine, Radiation Oncology, Biochemistry, Microbiology, Human Genetics, and Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA, USA
SOURCE:	Blood (2003), 102(10), 3765-3774 CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER:	American Society of Hematology
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Interactions between the proteasome inhibitor bortezomib and histone deacetylase inhibitors (HDIs) have been examined in Bcr/Abl+ human leukemia cells (K562 and LAMA 84). Coexposure of cells (24-48 h) to minimally toxic concns. of bortezomib + either suberoylanilide hydroxamic acid (SAHA) or sodium butyrate (SB) resulted in a striking increase in mitochondrial injury, caspase activation, and apoptosis, reflected by caspases-3 and -8 cleavage and poly(ADP-ribose) polymerase (PARP) degradation These events were accompanied by down-regulation of the Raf-1/mitogen-induced extracellular kinase (MEK)/extracellular signal-related kinase (ERK) pathway as well as diminished expression of Bcr/Abl and cyclin D1, cleavage of p21CIP1 and phosphorylation of the retinoblastoma protein (pRb), and induction of the stress-related kinases Jun kinase (JNK) and p38 mitogen-activated protein kinase (MAPK). Transient transfection of cells with a constitutively active MEK construct significantly protected them from bortezomib/SAHA-mediated lethality. Coadministration of bortezomib and SAHA resulted in increased reactive oxygen species (ROS) generation and diminished nuclear factor κB (NF-κB) activation; moreover, the free radical scavenger L-N-acetylcysteine (LNAC) blocked bortezomib/SAHA-related ROS generation, induction of JNK and p21CIP1, and apoptosis. Lastly, this regimen potently induced apoptosis in STI571 (imatinib mesylate)-resistant K562 cells and CD34+ mononuclear cells obtained from a patient with STI571-resistant disease, as well as in Bcr/Abl- leukemia cells (eg, HL-60, U937, Jurkat). Together, these findings raise the possibility that combined proteasome/histone deacetylase inhibition may represent a novel strategy in leukemia, including apoptosis-resistant Bcr/Abl+ hematol. malignancies.

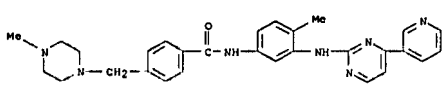
IT 220127-57-1, STI571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(proteasome inhibitor bortezomib interacts synergistically with histone deacetylase inhibitors to induce apoptosis in Bcr/Abl+ cells sensitive and resistant to STI571 in relation to signaling and survival pathways)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

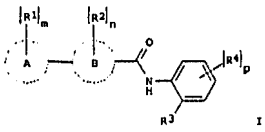
REFERENCE COUNT:	54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2003:892611 CAPLUS
DOCUMENT NUMBER:	139:381375
TITLE:	Preparation of amides as inhibitors of histone deacetylase
INVENTOR(S):	Stokes, Elaine Sophie Elizabeth; Waring, Michael James; Gibson, Keith Hopkinson
PATENT ASSIGNEE(S):	Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE:	PCT Int. Appl., 88 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003092686	A1	20031113	WO 2003-GB1703	20030417 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2484065	A1	20031113	CA 2003-2484065	20030417 <--
AU 2003226553	A1	20031117	AU 2003-226553	20030417 <--
EP 1501508	A1	20050202	EP 2003-747499	20030417
EP 1501508	B1	20070221		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009553	A	20050209	BR 2003-9553	20030417
CN 1662236	A	20050831	CN 2003-814828	20030417
JP 2005530748	T	20051013	JP 2004-500870	20030417
AT 354366	T	20070315	AT 2003-747499	20030417
IN 2004DN03153	A	20050401	IN 2004-DN3153	20041013
NO 2004004557	A	20041022	NO 2004-4557	20041022
US 2005222410	A1	20051006	US 2004-512808	20041026
PRIORITY APPLN. INFO.:			GB 2002-9715	A 20020427
			WO 2003-GB1703	W 20030417

OTHER SOURCE(S):	MARPAT 139:381375
GI	



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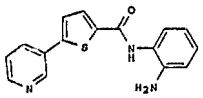


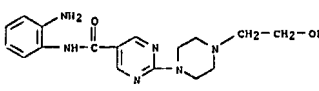
II

AB The title compds. [I; ring A = heterocyclyl; m = 0-4; R1 = OH, halo, CF3, CN; ring B = thienyl, thiadiazolyl, thiazolyl, pyrimidyl, pyrazinyl, pyridazinyl and pyridyl; R2 = halo; n = 0-2; R4 = OH, halo, CF3, CN; p = 0-4; R3 = NH2, OH] or pharmaceutically acceptable salts or in-vivo hydrolysable ester or amide thereof, useful in the treatment of diseases or medical conditions mediated by histone deacetylase such as cancer, were prepared Thus, coupling N-(2-tert-butoxycarbonylaminophenyl)-5-bromothiophene-2-carboxamide with pyridine-3-boronic acid in the presence of Pd(PPh3)4 followed by Boc-group removal afforded II. The compds. I showed IC50 of < 2.5 μM against recombinant human HDAC1 produced in Hi5 insect cells. The pharmaceutical compns. containing the compound I are claimed.

IT 623587-34-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amides as inhibitors of histone deacetylase)

RN 623587-34-8 CAPLUS

CN 5-Pyrimidinecarboxamide, N-(2-aminophenyl)-2-[4-(2-phenoxyethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

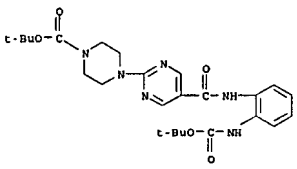


IT 623588-18-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amides as inhibitors of histone

deacetylase)

RN 623588-18-1 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[5-[[[2-[[(1,1-dimethylethoxy)carbonyl]amino]phenyl]amino]carbonyl]-2-pyrimidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:863816 CAPLUS

DOCUMENT NUMBER: 141:33398

TITLE: Mutations at amino-acid 482 in the ABCG2 gene affect substrate and antagonist specificity

AUTHOR(S): Robey, R. W.; Honjo, Y.; Morisaki, K.; Nadjem, T. A.; Runge, S.; Risbood, M.; Poruchynsky, M. S.; Bates, S. E.

CORPORATE SOURCE: Center for Cancer Research, Cancer Therapeutics Branch, National Institutes of Health, Bethesda, MD, 20892, USA

SOURCE: British Journal of Cancer (2003), 89(10), 1971-1978
CODEN: BJCAAI; ISSN: 0007-0920

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

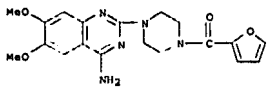
AB Recent studies have shown that mutations at amino-acid 482 in the ABCG2 gene affect the substrate specificity of the protein. To delineate the effects of these mutations clearly, human embryonic kidney cells (HEK-293) were stably transfected with wild-type 482R or mutant 482G and 482T ABCG2. By flow cytometry, mitoxantrone, BODIPY-prazosin, and Hoechst 33342 were found to be substrates of all ABCG2 proteins, while rhodamine 123, daunorubicin, and LysoTracker Green were transported only by mutant ABCG2. In cytotoxicity assays, all ABCG2 proteins conferred high levels of resistance to mitoxantrone, *SN*-38, and topotecan, while mutant ABCG2 also exhibited a gain of function for mitoxantrone as they conferred a four-fold greater resistance compared to wild type. Cells transfected with mutant ABCG2 were 13- to 71- fold resistant to the P-glycoprotein substrates doxorubicin, daunorubicin, epirubicin, bisantrene, and rhodamine 123 compared to cells transfected with wild-type ABCG2, which were only three- to four-fold resistant to these compds. ABCG2 did not confer appreciable resistance to etoposide, taxol or the histone deacetylase inhibitor depsipeptide. None of the transfected cell lines demonstrated resistance to flavopiridol despite our previous

observation that ABCG2-overexpressing cell lines are cross-resistant to the drug. Recently reported inhibitors of ABCG2 were evaluated and 50 μM novobiocin was found to reverse wild-type ABCG2 completely, but only reverse mutant ABCG2 partially. The studies presented here serve to underscore the importance of amino-acid 482 in defining the substrate specificity of the ABCG2 protein and raise the possibility that amino-acid 482 mutations in human cancers could affect the clin. application of antagonists for ABCG2.

IT 19216-56-9, Prazosin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mutations at amino-acid 482 in ABCG2 gene affect substrate and antagonist specificity)

RN 19216-56-9 CAPLUS

CN Methanone, [4-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl]-2-furanyl- (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:837045 CAPLUS

DOCUMENT NUMBER: 139:337995

TITLE: Preparation of benzamides as histone deacetylase inhibitors

INVENTOR(S): Stokes, Elaine Sophie Elizabeth; Roberts, Craig Anthony; Waring, Michael James

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

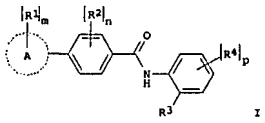
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003087057	A1	20031023	WO 2003-GB1442	20030402 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2480356	A1	20031023	CA 2003-2480356	20030402 <--
AU 2003217054	A1	20031027	AU 2003-217054	20030402 <--
BR 2003008875	A	20050104	BR 2003-8875	20030402

EP 1495002	A1	20050112	EP 2003-712442	20030402
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1642915	A	20050720	CN 2003-807431	20030402
US 2005171103	A1	20050804	US 2003-509941	20030402
JP 2005533011	T	20051104	JP 2003-584013	20030402
NZ 535143	A	20070427	NZ 2003-535143	20030402
IN 2004DN02719	A	20070302	IN 2004-DN2719	20040915
NO 2004004444	A	20041228	NO 2004-4444	20041019
PRIORITY APPLN. INFO.:			GB 2002-7863	A 20020405
			GB 2002-29930	A 20021221
			WO 2003-GB1442	W 20030402

OTHER SOURCE(S): MARPAT 139:337995

GI



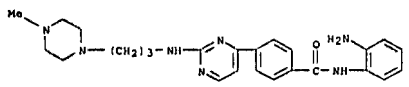
I

AB The title compds. [I; ring A = heterocyclyl; m = 0-4; R1 = OH, halo, CF3, CN, etc.; R2 = halo; n = 0-2; R3 = NH2, OH; R4 = OH, halo, CF3, CN, etc.; p = 0-4; or pharmaceutically-acceptable salts or in-vivo-hydrolysable esters or amides thereof], useful in the treatment of diseases or medical conditions mediated by histone deacetylase such as cancer, were prepared Thus, deprotection of N-(2-tert-butoxycarbonylaminophenyl)-4-(pyridin-4-yl)benzamide (preparation given) with 4M HCl solution in dioxane afforded 46% I.HCl [A = pyridin-4-yl; R2 = H; R3 = NH2; R4 = H]. The compds. I showed IC50 of < 50.0 μM in in vitro enzyme assay of pooled histone deacetylases. Pharmaceutical composition comprising the compound I is claimed.

IT 617702-12-2P 617702-23-5P 617702-37-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzamides as histone deacetylase inhibitors)

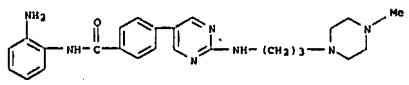
RN 617702-12-2 CAPLUS

CN Benzamide, N-(2-aminophenyl)-4-[2-[[3-(4-methyl-1-piperazinyl)propyl]amino]-4-pyrimidinyl]-, hydrochloride (9CI) (CA INDEX NAME)



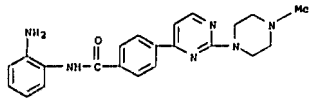
●x HCl

RN 617702-23-5 CAPLUS
CN Benzamide, N-(2-aminophenyl)-4-[2-[[3-(4-methyl-1-piperazinyl)propyl]amino]-5-pyrimidinyl]-, hydrochloride (9CI) (CA INDEX NAME)

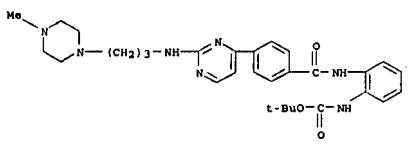


●x HCl

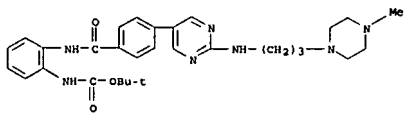
RN 617702-37-1 CAPLUS
CN Benzamide, N-(2-aminophenyl)-4-[2-(4-methyl-1-piperazinyl)-4-pyrimidinyl]- (9CI) (CA INDEX NAME)



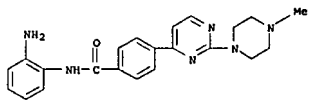
IT 617703-13-6P 617703-24-9P 617703-32-9P
617703-41-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzamides as histone deacetylase inhibitors)
RN 617703-13-6 CAPLUS
CN Carbamic acid, [2-[[4-[2-[[3-(4-methyl-1-piperazinyl)propyl]amino]-4-pyrimidinyl]benzoyl]amino]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 617703-24-9 CAPLUS
CN Carbamic acid, [2-[[4-[2-[[3-(4-methyl-1-piperazinyl)propyl]amino]-5-pyrimidinyl]benzoyl]amino]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

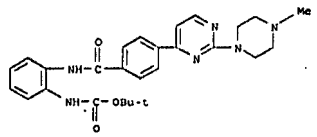


RN 617703-32-9 CAPLUS
CN Benzamide, N-(2-aminophenyl)-4-[2-(4-methyl-1-piperazinyl)-4-pyrimidinyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 617703-41-0 CAPLUS
CN Carbamic acid, [2-[[4-[2-(4-methyl-1-piperazinyl)-4-pyrimidinyl]benzoyl]amino]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:796490 CAPLUS
DOCUMENT NUMBER: 139:307794
TITLE: Preparation of N-hydroxy (piperazinesulfonyl)- or (piperazinecarbonyl)arylpropenamides as inhibitors of histone deacetylase and antiproliferative agents for the treatment of cancer and psoriasis
INVENTOR(S): Watkins, Clare J.; Romero-Martin, Maria-Rosario; Ritchie, James; Finn, Paul W.; Kalvinsh, Ivars; Loza, Einars; Dikovska, Klara; Starchenkov, Igor; Lolya, Daina; Gailite, Vija
PATENT ASSIGNEE(S): Prolifix Limited, UK
SOURCE: PCT Int. Appl., 217 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082288	A1	20031009	WO 2003-GB1463	20030403 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2479906	A1	20031009	CA 2003-2479906	20030403 <--
AU 2003229883	A1	20031013	AU 2003-229883	20030403 <--
BR 2003008908	A	20050104	BR 2003-8908	20030403
EP 1492534	A1	20050105	EP 2003-722719	20030403
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005143385	A1	20050630	US 2003-509732	20030403
JP 2005527556	T	20050915	JP 2003-579825	20030403
NZ 536116	A	20070126	NZ 2003-536116	20030403
NO 2004004744	A	20041102	NO 2004-4744	20041102
PRIORITY APPLN. INFO.:			US 2002-369337P	P 20020403

WO 2003-GB1463 W 20030403

OTHER SOURCE(S): MARPAT 139:307794
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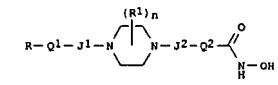

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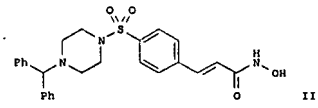
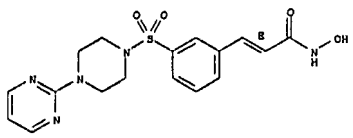


II

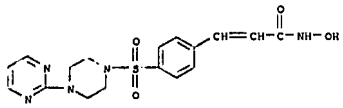
AB N-hydroxyamides I [J1 = single bond, C(:O), J2 = C(:O), SO2; Q1 = single bond, OX, SX, XOY, XSY, XO, XS; Q2 = (un)substituted C4-C8 alkylene at least four carbon atoms in length; R = (un)substituted cycloalkyl, heterocycloalkyl, or aryl; R1 = C1-C4 alkyl; X, Y = (un)substituted alkanediyl; n = 0-8] containing piperazine moieties, particularly N-hydroxy piperazinesulfonylarylpropenamides such as II, are prepared as inhibitors of histone deacetylase (HDAC) for the treatment of proliferative diseases, cancer, and psoriasis in both humans and animals. Biol. data on the inhibition of HDAC in vitro, the inhibition of cellular proliferation in vitro, and the in vivo testing of I on mice containing i.p. P388 tumors are given for a subset of I. Most of the compds. I tested inhibit HDAC with IC50 values between 20 nM and 200 nM, inhibit proliferation of four cell lines with IC50 values between 1 μM and 10 μM, and give log rank statistics for mice with P388 tumors (5 each) of between -3 and -5. II gives a log rank statistic for tumors in five mice of -9.62. Preparative data for approx. fifty of the title compds. are given.

IT 610801-39-3P 610801-49-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compds.; preparation of N-hydroxy (piperazinesulfonyl)- or (piperazinecarbonyl)arylpropenamides as inhibitors of histone deacetylase and antiproliferative agents for the treatment of cancer and psoriasis)
RN 610801-39-3 CAPLUS
CN 2-Propenamide, N-hydroxy-3-[3-[[4-(2-pyrimidinyl)-1-piperazinyl]sulfonyl]phenyl]-, (2E)- (9CI) (CA INDEX NAME)

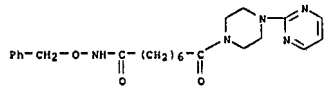
Double bond geometry as shown.



RN 610801-49-5 CAPLUS
CN 2-Propenamide, N-hydroxy-3-[4-[[4-(2-pyrimidinyl)-1-piperazinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)



IT 610802-53-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediates; preparation of N-hydroxy (piperazinesulfonyl)- or (piperazinecarbonyl)arylpropenamides as inhibitors of histone deacetylase and antiproliferative agents for the treatment of cancer and psoriasis)
RN 610802-53-4 CAPLUS
CN 1-Piperazineoctanamide, η-oxo-N-(phenylmethoxy)-4-(2-pyrimidinyl)- (9CI) (CA INDEX NAME)



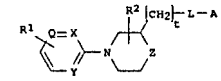
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737757 CAPLUS
DOCUMENT NUMBER: 139:276911
TITLE: Preparation of N-(piperazinylmethyl-, piperidinylmethyl- and morpholinylmethyl) sulfonamides and amides as novel inhibitors of histone deacetylase
INVENTOR(S): Van Emelen, Kristof

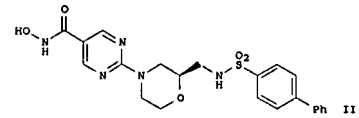
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076438	A1	20030918	WO 2003-EP2510	20030311 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475766	A1	20030918	CA 2003-2475766	20030311 <--
AU 2003218735	A1	20030922	AU 2003-218735	20030311 <--
EP 1485378	A1	20041215	EP 2003-711979	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007606	A	20041221	BR 2003-7606	20030311
CN 1642948	A	20050720	CN 2003-805921	20030311
US 2005165016	A1	20050728	US 2003-507084	20030311
JP 2005526766	T	20050908	JP 2003-574655	20030311
NZ 534833	A	20060728	NZ 2003-534833	20030311
IN 2004DN02536	A	20070413	IN 2004-DN2536	20040831
NO 2004004135	A	20040929	NO 2004-4135	20040929
PRIORITY APPLN. INFO.:			US 2002-363799P	P 20020313
			WO 2002-EP14833	A 20021223
			WO 2003-EP2510	W 20030311

OTHER SOURCE(S): MARPAT 139:276911
GI

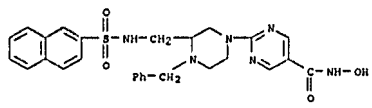


I

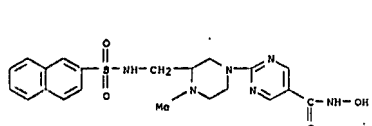


II

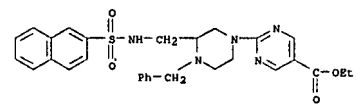
AB The title compds. [I; t = 0-4; Q, X, Y = N, C; Z = NH, O, CH2; R1 = CONR3R4, NHCOR7, CO(alkanediyl)SR7, etc. (wherein R3, R4 = H, OH, alkyl, etc.; R7 = H, alkyl, alkylcarbonyl, etc.); R2 = H, OH, NH2, etc.; L = NR9CO, NR9SO2, NR9CH2 (R9 = H, alkyl, cycloalkyl, etc.); A = (un)substituted Ph, cycloalkyl, pyridyl, etc.), having histone deacetylase inhibiting enzymic activity, were prepared and formulated. E.g., a multi-step synthesis of (+)-II which showed pIC50 of 7.723 against HDAC, was given.
IT 604784-81-8P 604784-91-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-(piperazinylmethyl-, piperidinylmethyl- and morpholinylmethyl) sulfonamides and amides as novel inhibitors of histone deacetylase)
RN 604784-81-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[3-[[(2-naphthalenylsulfonyl)amino]methyl]-4-(phenylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604784-91-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-methyl-3-[[(2-naphthalenylsulfonyl)amino]methyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



IT 604785-02-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-(piperazinylmethyl-, piperidinylmethyl- and morpholinylmethyl) sulfonamides and amides as novel inhibitors of histone deacetylase)
RN 604785-02-6 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[3-[[(2-naphthalenylsulfonyl)amino]methyl]-4-(phenylmethyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

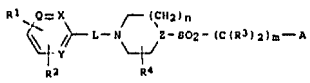
L7 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737742 CAPLUS
DOCUMENT NUMBER: 139:276884
TITLE: Preparation of sulfonyl-derivatives as novel inhibitors of histone deacetylase
INVENTOR(S): Van Emelen, Kristof; Arts, Janine; Backx, Leo Jacobus Jozef; De Winter, Hans Louis Jos; Van Brandt, Sven Franciscus Anna; Verdonck, Marc Gustaaf Celine; Meerpoel, Lieven; Pilatte, Isabelle Noeelle Constance; Poncelet, Virginie Sophie; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.; et al.
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076422	A1	20030918	WO 2003-EP2516	20030311 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2476586	A1	20030918	CA 2003-2476586	20030311 <--
AU 2003218738	A1	20030922	AU 2003-218738	20030311 <--
EP 1485365	A1	20041215	EP 2003-711982	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007575	A	20041221	BR 2003-7575	20030311
CN 1642931	A	20050720	CN 2003-805952	20030311
JP 2005525380	T	20050825	JP 2003-574641	20030311
NZ 534830	A	20050826	NZ 2003-534830	20030311
IN 2004DN02524	A	20070413	IN 2004-DN2524	20040830
US 2005113373	A1	20050526	US 2004-507708	20040913
US 7205304	B2	20070417		
NO 2004004314	A	20041012	NO 2004-4314	20041012
PRIORITY APPLN. INFO.:			US 2002-363799P	P 20020313
			US 2002-420989P	P 20021024

WO 2003-EP2516 W 20030311

OTHER SOURCE(S): MARPAT 139:276884

GI



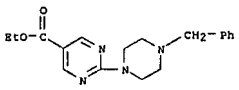
I

AB This invention comprises the novel compds. (I) (wherein n = 1-3, m = 1-4, Q, X, Y = N, CH; Z = N, CH; R1 = (un)substituted amido, acylamido, guandido, and other Zn chelating group, etc.; R2 = H, halo, OH, NH2, NO2, C1-6alkyl, C1-6alkoxy, CF3, di(C1-6alkyl)amino, HONH, naphthalenylsulfonylpyrazinyl; R3 = H aryl; R4 = H, HO, NH2, hydroxyC1-6alkyl, C1-6alkyl, C1-6alkoxy, arylC1-6alkyl, aminocarbonyl, hydroxycarbonyl, aminoC1-6alkyl, aminocarbonylC1-6alkyl, hydroxycarbonylC1-6alkyl, hydroxyaminocarbonyl, C1-6alkoxycarbonyl, C1-6alkylamino, di(C1-6alkyl)aminoC1-6alkyl; L = nul or bivalent radical selected from C1-6alkanediyl, amino, carbonyl or aminocarbonyl; A = aryl, cyclohexyl, heterocyclic derivs.), having histone deacetylase inhibiting enzymic activity; their preparation, compns. containing them and their use as a medicine. For example, 4-(4-[2-naphthylsulfonyl)piperazin-1-yl)-N-hydroxybenzamide in 100% yield was prepared by the hydrogenation of 4-(4-[2-naphthylsulfonyl)piperazin-1-yl)-N-(phenylmethoxy)benzamide (II) in THF by Pd/C as a catalyst. II was prepared from 1,1-dimethylethyl 4-(4-carboxyphenyl)-1-piperazinecarboxylate and O-(phenylmethyl)hydroxylamine hydrochloride in presence of dimethylaminopyridine in CH2Cl2 and diisopropylcarbodiimide, forming 1,1-dimethylethyl 4-[4-[(phenylmethoxy)amino]carbonylphenyl]-1-piperazinecarboxylate which was saponified and subsequently reacted with 2-naphthalenesulfonyl chloride to give the II.

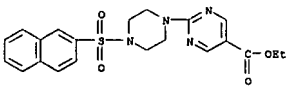
IT 603986-74-9P 604768-09-4P 604768-10-7P
604768-11-8P 604768-25-4P 604768-26-5P
604768-27-6P 604768-28-7P 604768-29-8P
604768-30-1P 604768-31-2P 604768-32-3P
604768-33-4P 604768-34-5P 604768-38-9P
604768-39-0P 604768-40-3P 604768-41-4P
604768-42-5P 604768-43-6P 604768-47-0P
604768-48-1P 604768-49-2P 604768-52-7P
604768-53-8P 604768-54-9P 604768-55-0P
604768-56-1P 604768-63-0P 604768-64-1P
604768-65-2P 604768-67-4P 604768-68-5P
604768-69-6P 604768-71-0P 604768-72-1P
604768-73-2P 604768-74-3P 604768-75-4P
604768-76-5P 604768-77-6P 604768-78-7P
604768-79-8P 604768-80-1P 604768-81-2P
604768-82-3P 604768-83-4P 604768-84-5P
604768-86-7P 604768-87-8P 604768-88-9P
604768-89-0P 604768-90-3P 604768-91-4P
604768-92-5P 604768-93-6P 604768-94-7P
604768-95-8P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of sulfonyl derivs. as histone deacetylase inhibitors and antitumor agent for treatment of cancer)

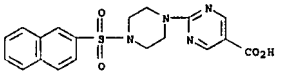
RN 603986-74-9 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-(phenylmethyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



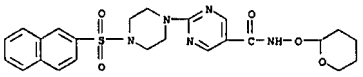
RN 604768-09-4 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



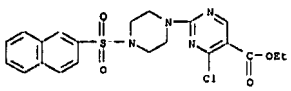
RN 604768-10-7 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



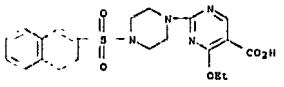
RN 604768-11-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



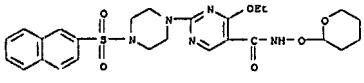
RN 604768-25-4 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



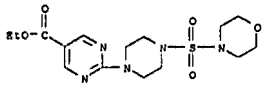
RN 604768-26-5 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 4-ethoxy-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



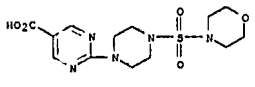
RN 604768-27-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 4-ethoxy-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



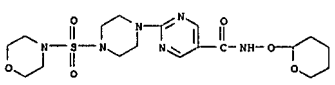
RN 604768-28-7 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-(4-morpholinylsulfonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



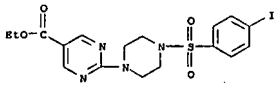
RN 604768-29-8 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-(4-morpholinylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



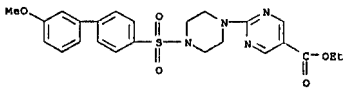
RN 604768-30-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(4-morpholinylsulfonyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



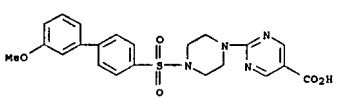
RN 604768-31-2 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[(4-iodophenyl)sulfonyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



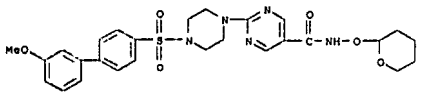
RN 604768-32-3 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[(3'-methoxy[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 604768-33-4 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[(3'-methoxy[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

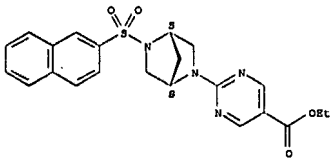


RN 604768-34-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3'-methoxy[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



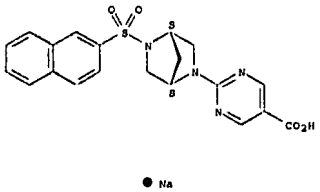
RN 604768-38-9 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[(1S,4S)-5-(2-naphthalenylsulfonyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



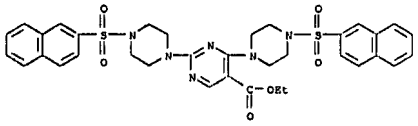
RN 604768-39-0 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[(1S,4S)-5-(2-naphthalenylsulfonyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]-, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

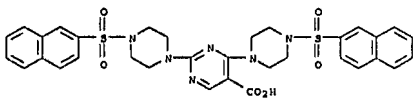


RN 604768-40-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[(1S,4S)-5-(2-naphthalenylsulfonyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 604768-48-1 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2,4-bis[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604768-49-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2,4-bis[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

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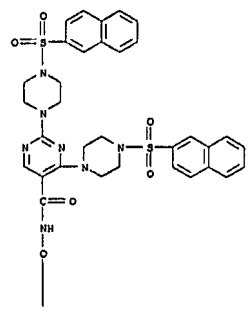
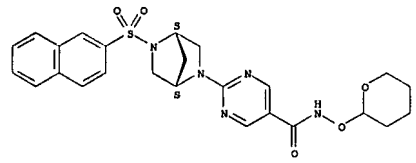
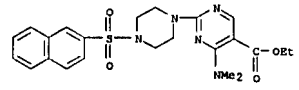
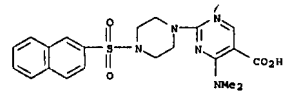




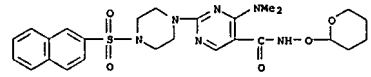
RN 604768-41-4 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 4-(dimethylamino)-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 604768-42-5 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 4-(dimethylamino)-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604768-43-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 4-(dimethylamino)-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



RN 604768-47-0 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2,4-bis[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)

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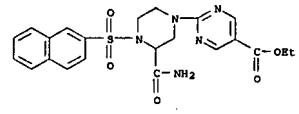
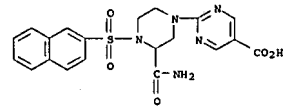
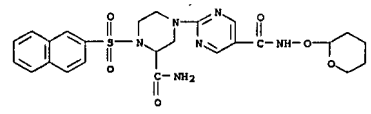
RN 604768-52-7 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[3-(aminocarbonyl)-4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



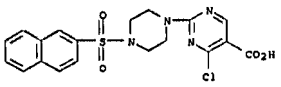
RN 604768-53-8 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[3-(aminocarbonyl)-4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



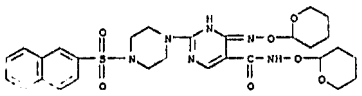
RN 604768-54-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[3-(aminocarbonyl)-4-(2-naphthalenylsulfonyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



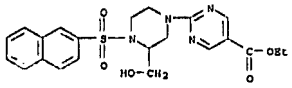
RN 604768-55-0 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



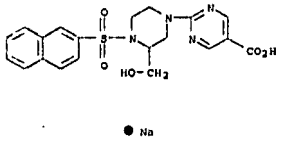
RN 604768-56-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]-4-[[(tetrahydro-2H-pyran-2-yl)oxy]amino]- (9CI) (CA INDEX NAME)



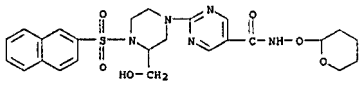
RN 604768-63-0 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[3-(hydroxymethyl)-4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



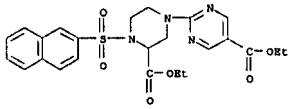
RN 604768-64-1 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[3-(hydroxymethyl)-4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, monosodium salt (9CI) (CA INDEX NAME)



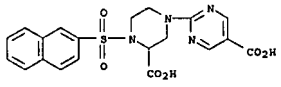
RN 604768-65-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[3-(hydroxymethyl)-4-(2-naphthalenylsulfonyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



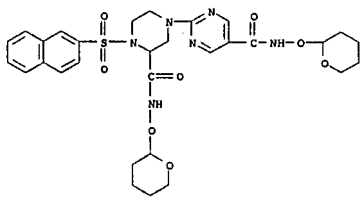
RN 604768-67-4 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[3-(ethoxycarbonyl)-4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



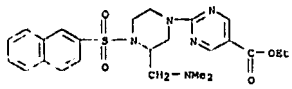
RN 604768-68-5 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[3-carboxy-4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



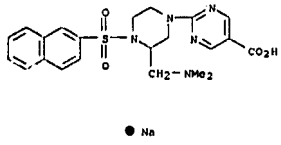
RN 604768-69-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(2-naphthalenylsulfonyl)-3-[[[(tetrahydro-2H-pyran-2-yl)oxy]amino]carbonyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



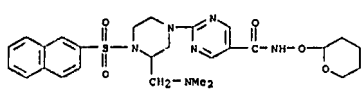
RN 604768-71-0 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[3-[(dimethylamino)methyl]-4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



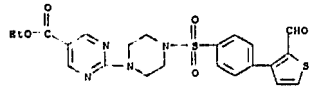
RN 604768-72-1 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[3-[(dimethylamino)methyl]-4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, sodium salt (9CI) (CA INDEX NAME)



RN 604768-73-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[3-[(dimethylamino)methyl]-4-(2-naphthalenylsulfonyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

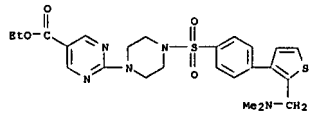


RN 604768-74-3 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[4-(2-formyl-3-thienyl)phenyl]sulfonyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)

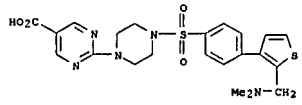


RN 604768-75-4 CAPLUS

CN 5-Pyrimidinecarboxylic acid, 2-[4-[[4-[2-[(dimethylamino)methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 604768-76-5 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[4-[2-[(dimethylamino)methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604768-77-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4-[2-[(dimethylamino)methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

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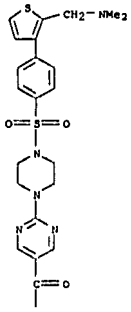

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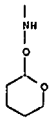
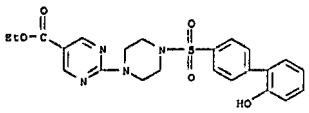
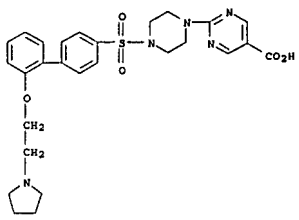


RN 604768-78-7 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[(2'-hydroxy[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)

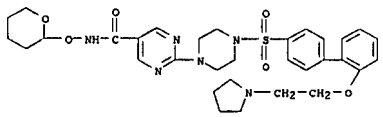


RN 604768-79-8 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[2'-[2-(1-pyrrolidinyl)ethoxy][1,1'-

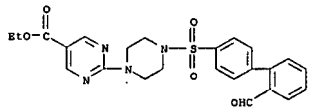
biphenyl]-4-yl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



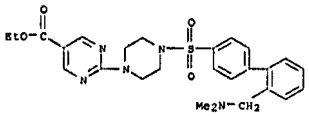
RN 604768-80-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[2'-[2-(1-pyrrolidinyl)ethoxy][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



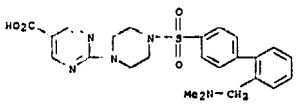
RN 604768-81-2 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[(2'-formyl[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



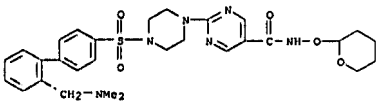
RN 604768-82-3 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[2'-[(dimethylamino)methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



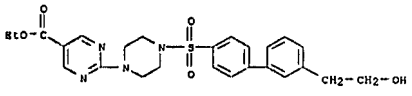
RN 604768-83-4 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[2'-[(dimethylamino)methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



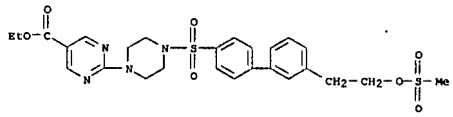
RN 604768-84-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[2'-[(dimethylamino)methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



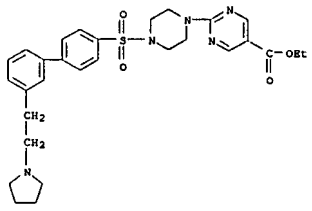
RN 604768-86-7 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[3'-(2-hydroxyethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



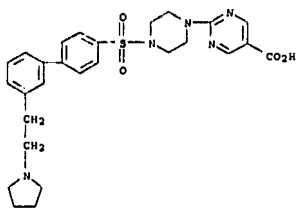
RN 604768-87-8 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[3'-[2-[(methylsulfonyl)oxy]ethyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 604768-88-9 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[3'-[2-(1-pyrrolidinyl)ethyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



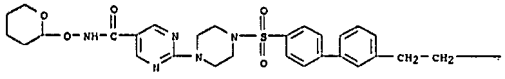
RN 604768-89-0 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[3'-[2-(1-pyrrolidinyl)ethyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, sodium salt (9CI) (CA INDEX NAME)



● Na

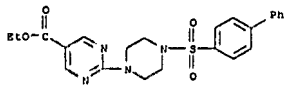
RN 604768-90-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[3'-[2-(1-pyrrolidinyl)ethyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

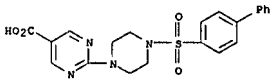


PAGE 1-B

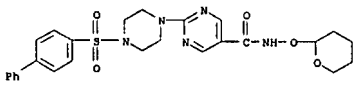
RN 604768-91-4 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-([1,1'-biphenyl]-4-ylsulfonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



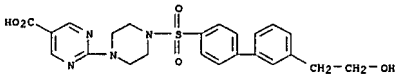
RN 604768-92-5 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-([1,1'-biphenyl]-4-ylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604768-93-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-([1,1'-biphenyl]-4-ylsulfonyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

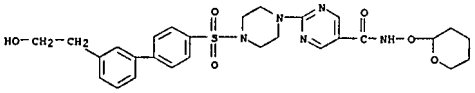


RN 604768-94-7 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[3'-(2-hydroxyethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 604768-95-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[3'-(2-hydroxyethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-((tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



IT 604769-01-9P 604769-07-5P 604769-08-6P

604769-09-7P 604769-10-0P 604769-12-2P
604769-13-3P 604769-15-5P 604769-16-6P
604769-17-7P 604769-19-9P 604769-20-3P
604769-21-3P 604769-22-4P 604769-23-5P
604769-24-6P 604769-25-7P 604769-26-8P
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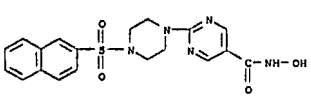
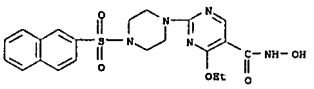
604771-60-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonyl deriva. as histone deacetylase inhibitors and antitumor agent for treatment of cancer)

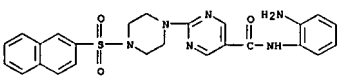
RN 604769-01-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



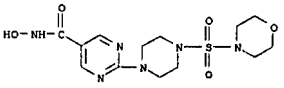
RN 604769-07-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 4-ethoxy-N-hydroxy-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



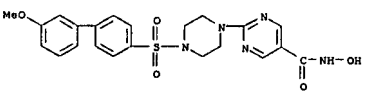
RN 604769-08-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-(2-aminophenyl)-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604769-09-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(4-morpholinylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

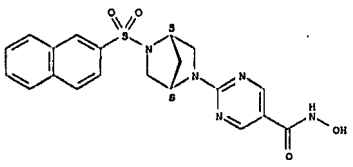


RN 604769-10-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(3'-methoxy[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

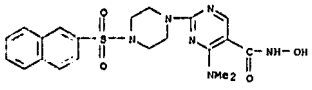


RN 604769-12-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[(1S,4S)-5-(2-naphthalenylsulfonyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]- (9CI) (CA INDEX NAME)

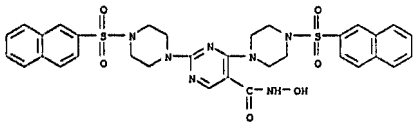
Absolute stereochemistry.



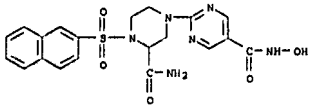
RN 604769-13-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 4-(dimethylamino)-N-hydroxy-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604769-15-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2,4-bis[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

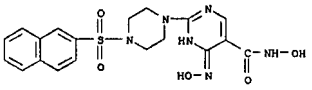


RN 604769-16-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[3-(aminocarbonyl)-4-(2-naphthalenylsulfonyl)-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)

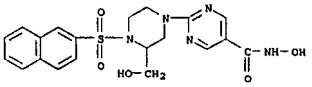


RN 604769-17-7 CAPLUS

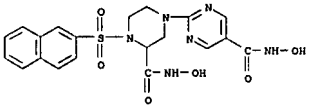
CN 5-Pyrimidinecarboxamide, N-hydroxy-4-(hydroxyamino)-2-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



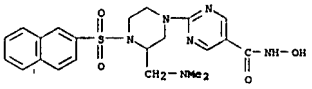
RN 604769-19-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[3-(hydroxymethyl)-4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



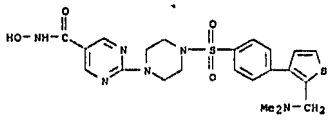
RN 604769-20-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[3-[(hydroxyamino)carbonyl]-4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



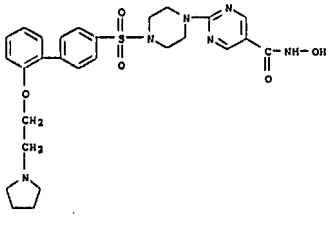
RN 604769-21-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[3-[(dimethylamino)methyl]-4-(2-naphthalenylsulfonyl)-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



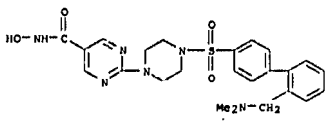
RN 604769-22-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4-[2-[(dimethylamino)methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



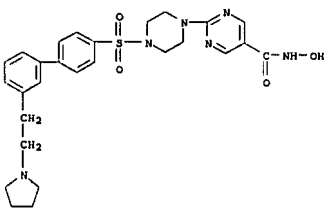
RN 604769-23-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[2'-[2-(1-pyrrolidinyl)ethoxy][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



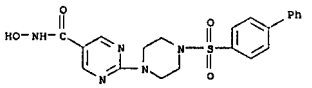
RN 604769-24-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[2'-[(dimethylamino)methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



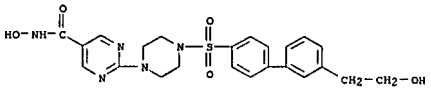
RN 604769-25-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[3'-[2-(1-pyrrolidinyl)ethyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604769-26-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-([1,1'-biphenyl]-4-ylsulfonyl)-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



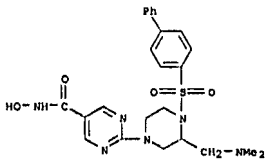
RN 604769-27-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[3'-(2-hydroxyethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604770-13-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-([1,1'-biphenyl]-4-ylsulfonyl)-3-[(dimethylamino)methyl]-1-piperazinyl]-N-hydroxy-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-12-9
CMF C24 H28 N6 O4 S



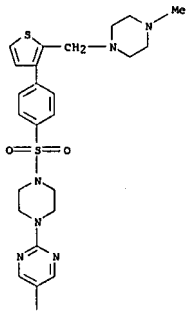
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-15-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[2-[(4-methyl-1-piperazinyl)methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-14-1
CMF C25 H31 N7 O4 S2



CM 2

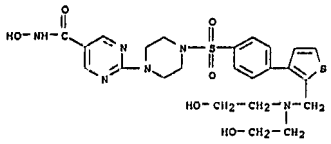
CRN 76-05-1
CMF C2 H F3 O2

RN 604770-17-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4-[2-[[bis(2-hydroxyethyl)amino]methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-16-3

CMF C24 H30 N6 O6 S2



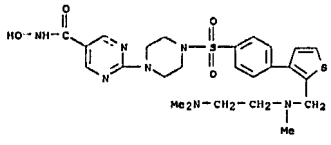
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-19-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4-[2-[[[2-(dimethylamino)ethyl]methylamino]methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-18-5
CMF C25 H33 N7 O4 S2



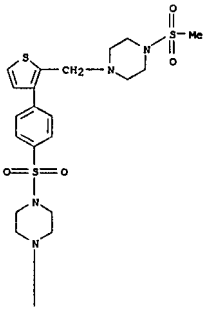
CM 2

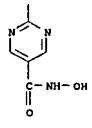
CRN 76-05-1
CMF C2 H F3 O2

RN 604770-21-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[2-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-20-9
CMF C25 H31 N7 O6 S3





CM 2

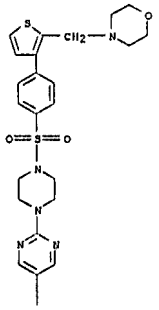
CRN 76-05-1
CMF C2 H F3 O2

RN 604770-23-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[2-(4-morpholinylmethyl)-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-22-1
CMF C24 H28 N6 O5 S2

PAGE 1-A



PAGE 2-A

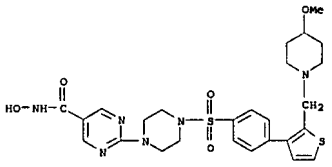
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-25-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[2-[(4-methoxy-1-piperidinyl)methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-24-3
CMF C26 H32 N6 O5 S2



CM 2

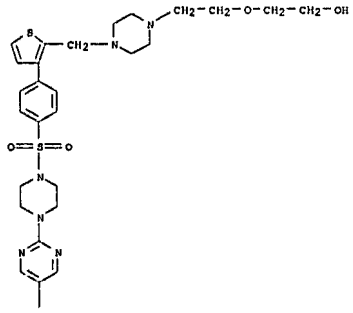
CRN 76-05-1
CMF C2 H F3 O2

RN 604770-27-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[2-[[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-26-5
CMF C28 H37 N7 O6 S2

PAGE 1-A



PAGE 2-A

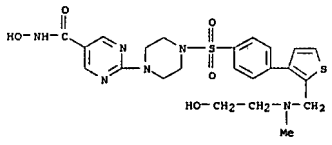
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-29-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[2-[[[2-hydroxyethyl)methylamino]methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-28-7
CMF C23 H28 N6 O5 S2



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-31-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[2-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-3-thienyl]phenyl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-30-1
CMF C26 H33 N7 O5 S2

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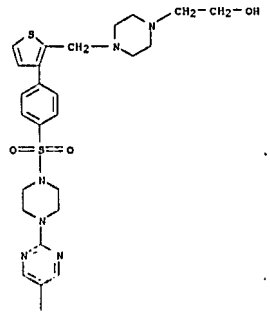


PAGE 2-A

CM 2

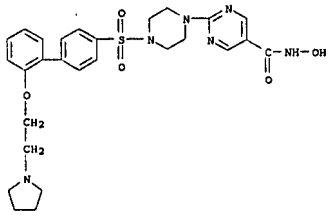
CRN 76-05-1
CMF C2 H F3 O2

RN 604770-32-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[2'-[2-(1-pyrrolidinyl)ethoxy][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604769-23-5

CMF C27 H32 N6 O5 S



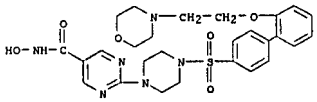
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-34-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[2'-[2-(4-morpholinyl)ethoxy][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-33-4
CMF C27 H32 N6 O6 S



CM 2

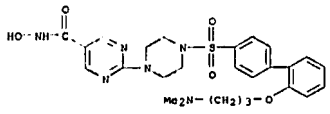
CRN 76-05-1

CMF C2 H F3 O2

RN 604770-36-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[2'-(3-(dimethylamino)propoxy)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl)-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-35-6
CMF C26 H32 N6 O5 S



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-38-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4'-[2-(1-pyrrolidinyl)ethoxy][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-37-8
CMF C27 H32 N6 O5 S

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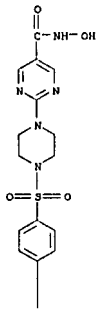
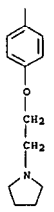


PAGE 2-A



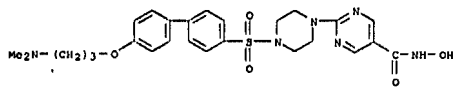
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-40-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4'-[3-(dimethylamino)propoxy][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy-, trifluoroacetate (5:6) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-39-0
CMF C26 H32 N6 O5 S



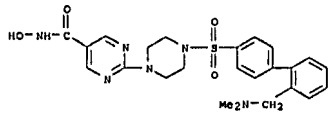
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-41-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[2'-[(dimethylamino)methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604769-24-6
CMF C24 H28 N6 O4 S



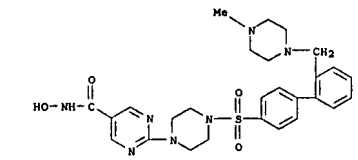
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-43-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[2'-[(4-methyl-1-piperazinyl)methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, trifluoroacetate (5:6) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-42-5
CMF C27 H33 N7 O4 S



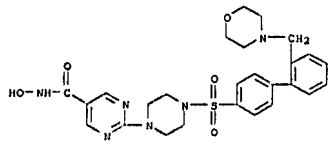
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-45-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[2'-(4-morpholinylmethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-44-7
CMF C26 H30 N6 O5 S



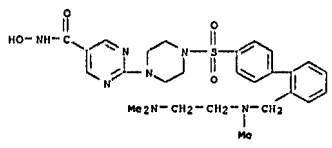
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-47-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[2'-[[[2-(dimethylamino)ethyl]methylamino]methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy-, trifluoroacetate (2:3) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-46-9
CMF C27 H35 N7 O4 S



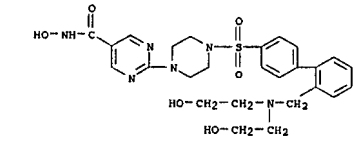
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-49-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[2'-[[bis(2-hydroxyethyl)amino]methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-48-1
CMF C26 H32 N6 O6 S



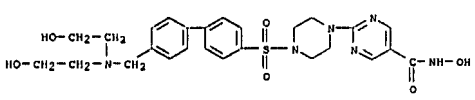
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-51-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4'-[[bis(2-hydroxyethyl)amino]methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-50-5
CMF C26 H32 N6 O6 S



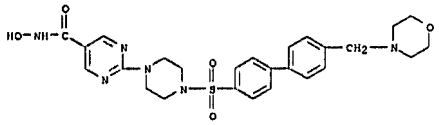
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-53-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4'-(4-morpholinylmethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-52-7
CMF C26 H30 N6 O5 S



CM 2

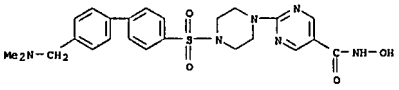
CRN 76-05-1
CMF C2 H F3 O2

RN 604770-55-0 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-[4-[[4'-[(dimethylamino)methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-54-9
CMF C24 H28 N6 O4 S



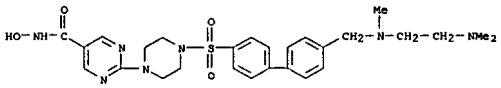
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-57-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4'-[[[2-(dimethylamino)ethyl]methylamino]methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy-, trifluoroacetate (2:3) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-56-1
CMF C27 H35 N7 O4 S



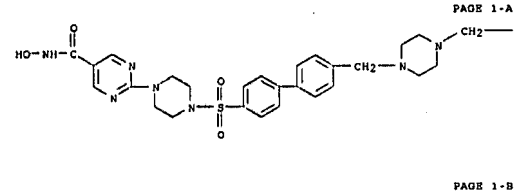
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-59-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4'-[[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-58-3
CMF C30 H39 N7 O6 S



—CH_2—O—CH_2—CH_2—OH

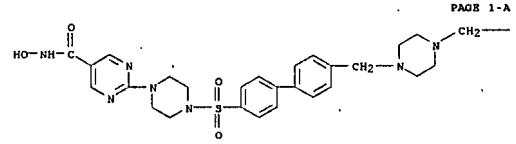
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-61-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4'-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-60-7
CMF C28 H35 N7 O5 S



—CH_2—OH

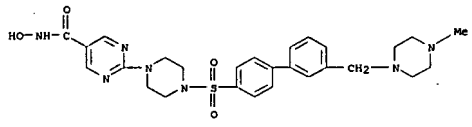
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-63-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[3'-[(4-methyl-1-piperazinyl)methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, trifluoroacetate (10:11) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-62-9
CMF C27 H33 N7 O4 S



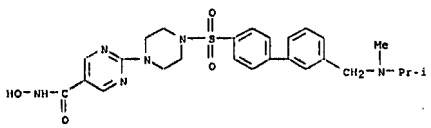
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-65-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[3'-[[methyl(1-methylethyl)amino]methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-64-1
CMF C26 H32 N6 O4 S



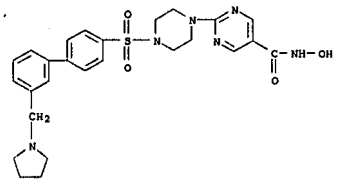
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-67-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[3'-(1-pyrrolidinylmethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-66-3
CMF C26 H30 N6 O4 S



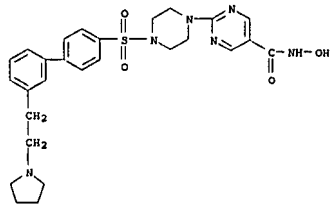
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-68-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[3'-[2-(1-pyrrolidinyl)ethyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604769-25-7
CMF C27 H32 N6 O4 S



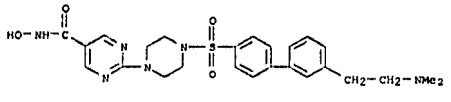
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-70-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[3'-(2-(dimethylamino)ethyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-69-6
CMF C25 H30 N6 O4 S



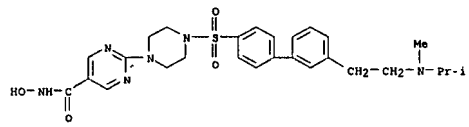
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-72-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[3'-[2-[methyl(1-methylethyl)amino]ethyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604770-71-0
CMF C27 H34 N6 O4 S



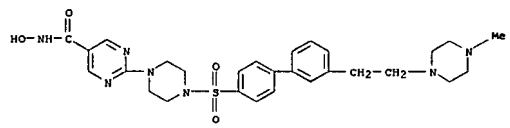
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604770-74-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[3'-[2-(4-methyl-1-piperazinyl)ethyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

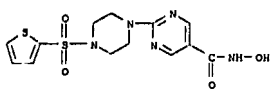
CRN 604770-73-2
CMF C28 H35 N7 O4 S



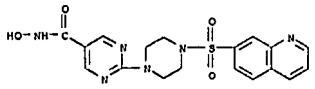
CM 2

CRN 76-05-1
CMF C2 H F3 O2

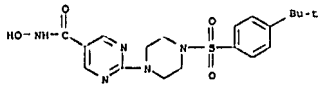
RN 604770-97-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-thienylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



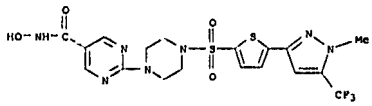
RN 604770-98-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(7-quinolinylsulfonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



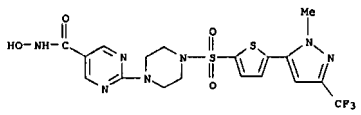
RN 604770-99-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



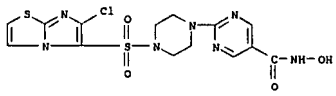
RN 604771-00-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl]-2-thienyl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



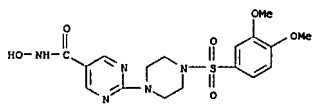
RN 604771-01-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]-2-thienyl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



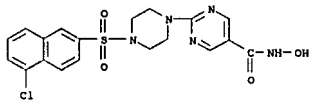
RN 604771-02-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(6-chloroimidazo[2,1-b]thiazol-5-yl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



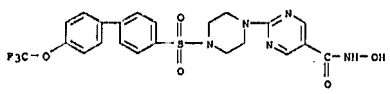
RN 604771-03-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3,4-dimethoxyphenyl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



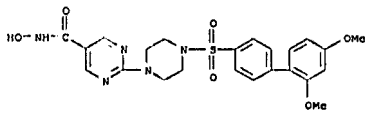
RN 604771-04-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(5-chloro-2-naphthalenyl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



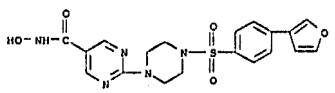
RN 604771-05-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



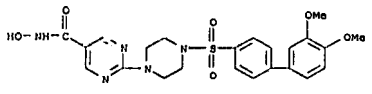
RN 604771-06-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(2',4'-dimethoxy[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



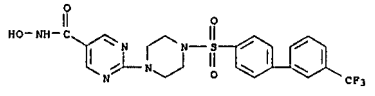
RN 604771-07-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4-(3-furanyl)phenyl]sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



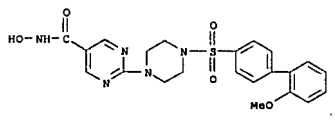
RN 604771-08-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3',4'-dimethoxy[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



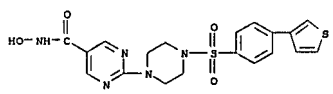
RN 604771-09-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[3'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



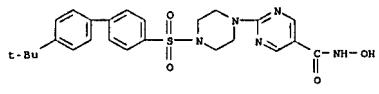
RN 604771-10-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2'-methoxy[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



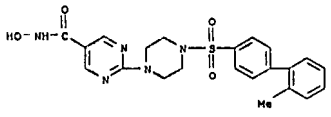
RN 604771-11-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-(3-thienyl)phenyl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



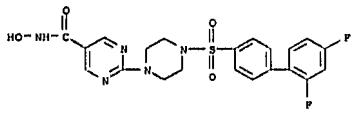
RN 604771-12-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4'-(1,1-dimethylethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



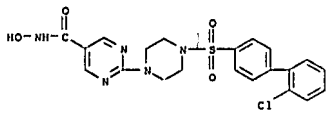
RN 604771-13-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2'-methyl[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



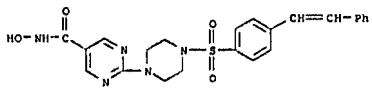
RN 604771-14-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(2',4'-difluoro[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



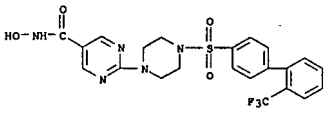
RN 604771-15-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(2'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 604771-16-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-(2-phenylethenyl)phenyl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604771-17-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604771-18-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-(8-quinolinyl)phenyl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

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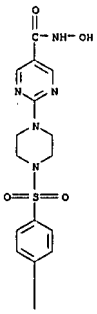

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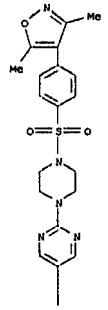
RN 604771-19-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4-(3,5-dimethyl-4-isoxazolyl)phenyl]sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)

PAGE 1-A



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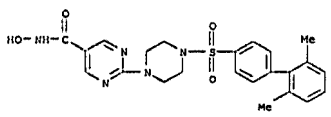
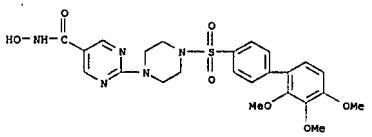
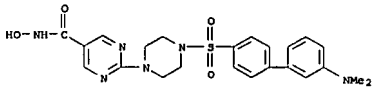
RN 604771-20-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(2',6'-dimethyl[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



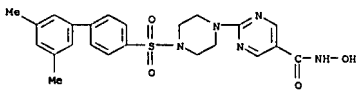
RN 604771-21-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2',3',4'-trimethoxy[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



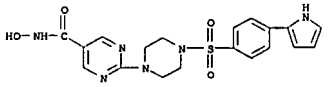
RN 604771-22-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[3'-(dimethylamino)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



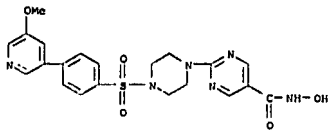
RN 604771-23-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3',5'-dimethyl[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



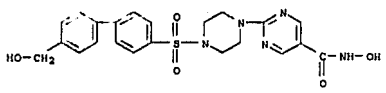
RN 604771-24-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-(1H-pyrrol-2-yl)phenyl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



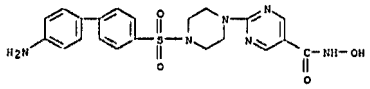
RN 604771-25-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-(5-methoxy-3-pyridinyl)phenyl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604771-26-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



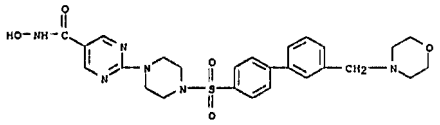
RN 604771-27-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(4'-amino[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 604771-29-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[3'-(4-morpholinylmethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 604771-28-0
CMF C26 H30 N6 O5 S



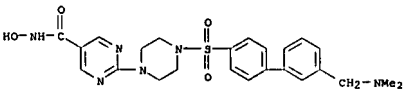
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 604771-31-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[3'-[(dimethylamino)methyl][1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

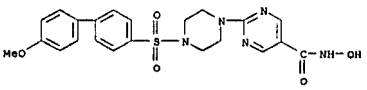
CRN 604771-30-4
CMF C24 H28 N6 O4 S



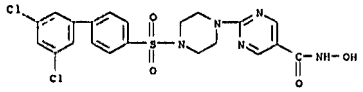
CM 2

CRN 76-05-1
CMF C2 H F3 O2

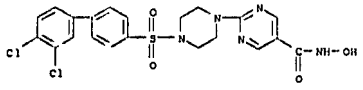
RN 604771-32-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(4'-methoxy[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



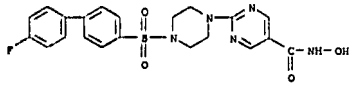
RN 604771-33-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3',5'-dichloro[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



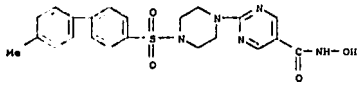
RN 604771-34-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3',4'-dichloro[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



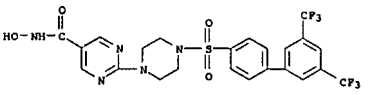
RN 604771-35-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(4'-fluoro[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



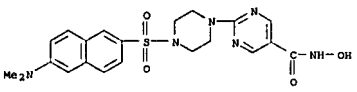
RN 604771-36-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(4'-methyl[1,1'-biphenyl]-4-yl)sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



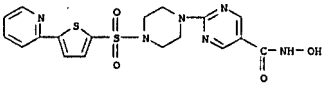
RN 604771-37-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[3',5'-bis(trifluoromethyl)[1,1'-biphenyl]-4-yl]sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 604771-38-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[6-(dimethylamino)-2-naphthalenyl]sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 604771-39-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-(2-pyridinyl)-2-thienyl]sulfonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 604771-40-6 CAPLUS
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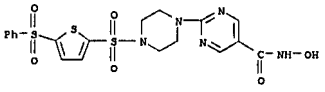

RN 604771-41-7 CAPLUS
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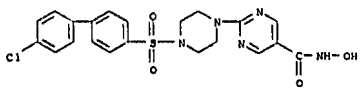

RN 604771-42-8 CAPLUS
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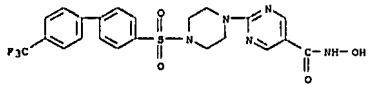

RN 604771-43-9 CAPLUS
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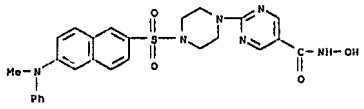
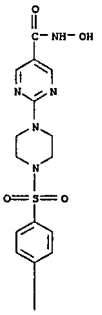


RN 604771-57-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[[4-(4-dibenzothienyl)phenyl]sulfonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)

PAGE 1-A



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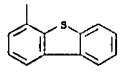

RN 604771-59-7 CAPLUS
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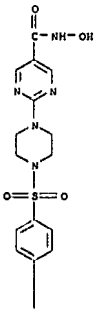
PAGE 1-A



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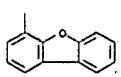

RN 604771-60-0 CAPLUS
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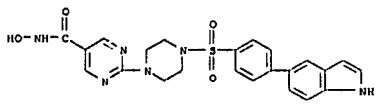


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

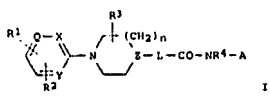
L7 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737741 CAPLUS
DOCUMENT NUMBER: 139:261323
TITLE: Preparation of aminocarbonyl derivatives as inhibitors

of histone deacetylase
INVENTOR(S): Van Emelen, Kristof; De Winter, Hans Louis Jos; Dyatkin, Alexey Borisovich; Verdonck, Marc Gustaaf Celine; Meerpoel, Lieven
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076421	A1	20030918	WO 2003-EP2511	20030311 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2476583	A1	20030918	CA 2003-2476583	20030311 <--
AU 2003212335	A1	20030922	AU 2003-212335	20030311 <--
EP 1485364	A1	20041215	EP 2003-708214	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1639125	A	20050713	CN 2003-805675	20030311
CN 1642551	A	20050720	CN 2003-805833	20030311
JP 2005523907	T	20050811	JP 2003-574640	20030311
ZA 2004007237	A	20050928	ZA 2004-7237	20040909
ZA 2004007235	A	20051004	ZA 2004-7235	20040909
US 2005222414	A1	20051006	US 2004-507271	20040909
ZA 2004007232	A	20051006	ZA 2004-7232	20040909
ZA 2004007233	A	20051006	ZA 2004-7233	20040909
ZA 2004007234	A	20051006	ZA 2004-7234	20040909
ZA 2004007236	A	20051006	ZA 2004-7236	20040909

PRIORITY APPLN. INFO.: US 2002-363799P P 20020313
WO 2003-EP2511 W 20030311

OTHER SOURCE(S): MARPAT 139:261323
GI



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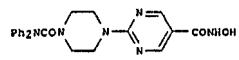
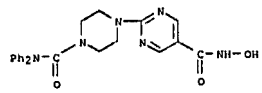


II

AB The title compds. I (Q, X, Y = N, (un)substituted CH; R1 = (un)substituted CONH2, NHCHO, COalkanediylSH, CONHOH, NHCOC:NHOH or other Zn-chelating group; R2 = H, halogen, OH, amino, NO2, alkyl, alkoxy, CF3, dialkylamino, NHOH, naphthalenylsulfonylpyrazinyl; R3 = H, OH, amino, (un)substituted alkyl, alkoxy, CONH2, CO2H; R4 = H, alkyl, cycloalkyl, hydroxyalkyl, alkoxyalkyl, dialkylaminoalkyl, aryl; L = bond, NH, alkanediylamino; A = (un)substituted Ph, cyclohexyl, heterocyclic, heteroaryl, naphthyl; n = 0-3] were prepared for use as histone deacetylase inhibitors in the treatment of proliferative diseases. Thus, the carbamoylpiperazinylpyrimidinecarboxamide II was prepared from piperazine, Et 5-methylsulfonylpyrimidine-2-carboxylate, and Ph2NCOCl in 5 steps. II had pIC50 for inhibition of histone deacetylase of 7.127 and for antiproliferative activity against A2780 cells of 6.114.

IT 603964-87-0P 603964-89-2P 603965-73-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinecarboxamide derivs. as novel inhibitors of histone deacetylase)

RN 603964-87-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(diphenylamino)carbonyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 603964-89-2 CAPLUS
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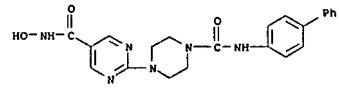
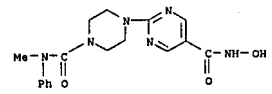
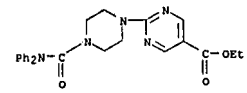


RN 603965-73-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(methylphenylamino)carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



IT 603965-78-2P 603965-79-3P 603965-80-6P 603965-84-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazinecarboxamide derivs. as novel inhibitors of histone deacetylase)

RN 603965-78-2 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[(diphenylamino)carbonyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 603965-79-3 CAPLUS
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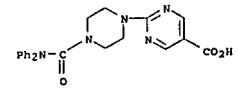

RN 603965-80-6 CAPLUS
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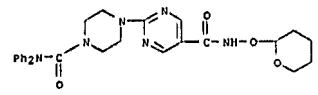

RN 603965-84-0 CAPLUS
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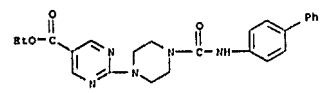

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737724 CAPLUS
DOCUMENT NUMBER: 139:276820
TITLE: Preparation of sulfonylaminopiperidine derivatives as inhibitors of histone deacetylase
INVENTOR(S): Van Emelen, Kristof; Backx, Leo Jacobus Jozef; Van Brandt, Sven Franciscus Anna; Angibaud, Patrick Rene; Pilatte, Isabelle Noelle Constance; Verdonck, Marc Gustaaf Celine; De Winter, Hans Louis Jos
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076401	A1	20030918	WO 2003-EP2517	20030311 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003209727	A1	20030922	AU 2003-209727	20030311 <--

EP 1485354	A1	20041215	EP 2003-743874		20030311
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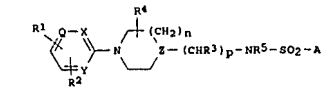
BR 2003007599	A	20050201	BR 2003-7599		20030311
CN 1642912	A	20050720	CN 2003-805951		20030311
US 2005171347	A1	20050804	US 2003-507159		20030311
JP 2005526763	T	20050908	JP 2003-574622		20030311
NZ 534771	A	20060428	NZ 2003-534771		20030311
IN 2004DN02521	A	20070112	IN 2004-DN2521		20040830
NO 2004004224	A	20041005	NO 2004-4224		20041005
PRIORITY APPLN. INFO.:			US 2002-363799P	P	20020313
			WO 2002-EP14481	A	20021218
			WO 2002-EP14081	A	20021218
			WO 2003-EP2517	W	20030311

OTHER SOURCE(S): MARPAT 139:276820
GI



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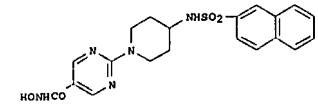


II

AB The title compds. I (Q, X, Y, Z = N, (un)substituted CH; R1 = (un)substituted CONH2, NHCHO, COalkanediylSH, CONHOH, NHCOC:NHOH or other Zn-chelating group; R2 = H, halogen, OH, amino, NO2, alkyl, alkoxy, CF3, dialkylamino, NHOH, naphthalenylsulfonylpyrazinyl; R3 = H, aryl; R4 = H, OH, amino, (un)substituted alkyl, alkoxy, CONH2, CO2H; R5 = H, alkyl, cycloalkyl, hydroxyalkyl, alkoxyalkyl, dialkylaminoalkyl, aryl; A = (un)substituted Ph, cyclohexyl, heterocyclic, heteroaryl, naphthyl; n = 0-3; p = 0-4] were prepared for use as histone deacetylase inhibitors in the treatment of proliferative diseases. Thus, the sulfonylaminopiperidine II was prepared from Et 4-aminopiperidine-1-carboxylate, 2-naphthalenesulfonyl chloride, and Et 2-methylsulfonylpyrimidine-5-carboxylate in 6 steps. II had pIC50 for inhibition of histone deacetylase of 6.523 and for antiproliferative activity against A2780 cells of 5.277.

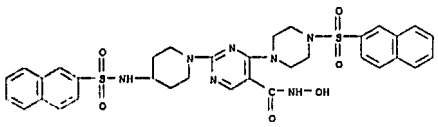
IT 603953-72-6P 603954-03-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonylaminopiperidine derivs. as inhibitors of histone deacetylase)

RN 603953-72-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2-naphthalenylsulfonyl)amino]-1-

piperidinyl]-4-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603953-71-5
CMF C34 H35 N7 O6 S2



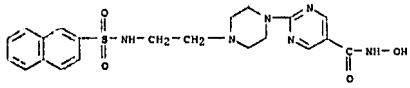
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 603954-03-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-[(2-naphthalenylsulfonyl)amino]ethyl]-1-piperazinyl]-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603954-02-5
CMF C21 H24 N6 O4 S



CM 2

CRN 76-05-1
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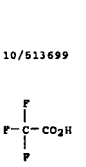
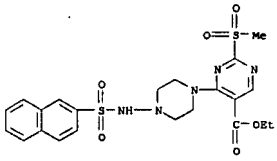
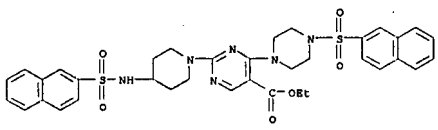


IT 603954-28-5P 603954-64-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of sulfonylaminopiperidine derivs. as inhibitors of histone deacetylase)

RN 603954-28-5 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-(methylsulfonyl)-4-[4-[(2-naphthalenylsulfonyl)amino]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 603954-64-9 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[(2-naphthalenylsulfonyl)amino]-1-piperidinyl]-4-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737723 CAPLUS
DOCUMENT NUMBER: 139:261309
TITLE: Preparation of N-hydroxy-5-piperazino(piperidino or diazepino)-2-pyrimidinecarboxamides and N-hydroxy-4-piperazino(piperidino or

diazepino)benzamides as new inhibitors of histone deacetylase
INVENTOR(S): Angibaud, Patrick Rene; Pilatte, Isabelle Noeelle Constance; Van Brandt, Sven Franciscus Anna; Roux, Bruno; Ten Holte, Peter; Verdonck, Marc Gustaaf Celine; Meerpoel, Lieven; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076400	A1	20030918	WO 2003-EP2514	20030311 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475764	A1	20030918	CA 2003-2475764	20030311 <--
AU 2003218736	A1	20030922	AU 2003-218736	20030311 <--
EP 1485353	A1	20041215	EP 2003-711980	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008081	A	20041221	BR 2003-8081	20030311
US 2005107384	A1	20050519	US 2003-506998	20030311
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CN 1642551	A	20050720	CN 2003-805833	20030311
NZ 534834	A	20050729	NZ 2003-534834	20030311
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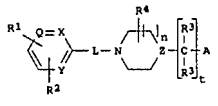
NO 2004004194	A	20041001	NO 2004-4194	20041001
PRIORITY APPLN. INFO.:			US 2002-363799P P	20020313
			WO 2003-EP2514 W	20030311

OTHER SOURCE(S): MARPAT 139:261309
GI



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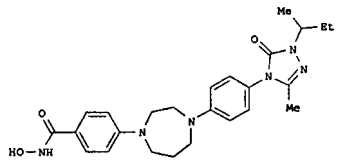


II

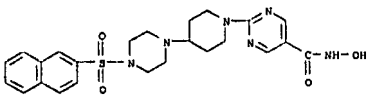
AB The title compds. [I; n = 0-3; t = 0-4; Q, X, Y = N, C; Z = N, CH; R1 = CONR7R8, NHCOR9, CO(alkanediyl)SR9, etc. (wherein R7, R8 = H, OH, alkyl, etc.; R9 = H, alkyl, alkylcarbonyl, etc.); R2 = H, halo, OH, etc.; L = a bond, alkanediyl, alkanediyloxy, NH, CO, NHCO; each R3 = H and one H atom can be replaced by aryl; R4 = H, OH, NH2, etc.; A = (un)substituted Ph, cyclohexyl, pyridyl, etc.], having histone deacetylase inhibiting enzymic activity, were prepared and formulated. E.g., a multi-step synthesis of II which showed pIC50 of 5.121 against HDAC, was given.

IT 603985-85-9P 603985-87-1P 603985-89-3P
603985-91-7P 603985-95-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazino(piperidino or diazepino) substituted 2-pyrimidinecarbohydroxamic acids and N-hydroxybenzamides as new inhibitors of histone deacetylase)

RN 603985-85-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-1-piperidinyl]-, trifluoroacetate (10:9) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603985-84-8
CMF C24 H28 N6 O4 S



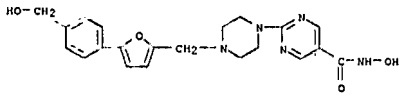
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 603985-87-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, trifluoroacetate (5:4) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603985-86-0
CMF C21 H23 N5 O4



CM 2

CRN 76-05-1
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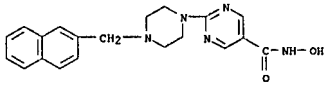
RN 603985-89-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-

piperazinyl]-, trifluoroacetate (5:4) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603985-88-2
CMF C20 H21 N5 O2



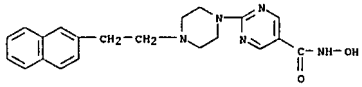
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 603985-91-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-(2-naphthalenyl)ethyl]-1-piperazinyl]-, trifluoroacetate (5:4) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603985-90-6
CMF C21 H23 N5 O2



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 603985-95-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603985-94-0
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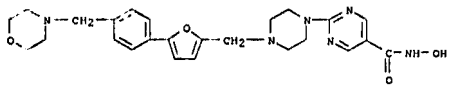
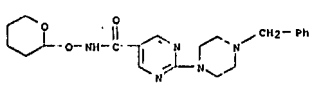


CM 2

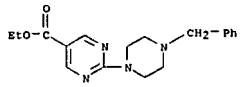
CRN 76-05-1
CMF C2 H F3 O2

IT 603986-73-8P 603986-74-9P 603986-83-0P
603986-88-5P 603986-89-6P 603986-90-9P
603986-91-0P 603986-92-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazino(piperidino or diazepino) substituted 2-pyrimidinecarbohydroxamic acids and N-hydroxybenzamides as new inhibitors of histone deacetylase)

RN 603986-73-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(phenylmethyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



RN 603986-74-9 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-(phenylmethyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 603986-83-0 CAPLUS
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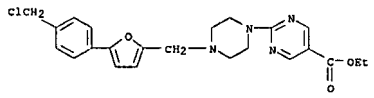
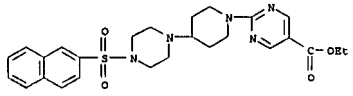
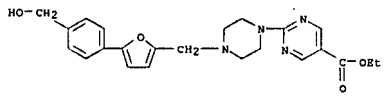


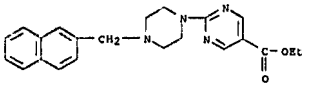
RN 603986-88-5 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-1-piperidinyl]-, ethyl ester (9CI) (CA INDEX NAME)



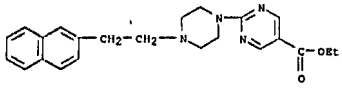
RN 603986-89-6 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



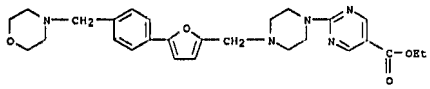
RN 603986-90-9 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-(2-naphthalenylmethyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 603986-91-0 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[2-(2-naphthalenyl)ethyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 603986-92-1 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737586 CAPLUS
DOCUMENT NUMBER: 139:261308
TITLE: Preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases
INVENTOR(S): Van Emelen, Kristof; Verdonck, Marc Gustaaf Celine; Van Brandt, Sven Franciscus Anna; Angibaud, Patrick Rene; Meerpoel, Lieven; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076929	A1	20030918	WO 2003-EP2515	20030311 <--

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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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ZA 2004007237	A	20050928	ZA 2004-7237	20040909
ZA 2004007235	A	20051004	ZA 2004-7235	20040909
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NO 2004004113	A	20040928	NO 2004-4113	20040928
PRIORITY APPLN. INFO.:			US 2002-363799P	P 20020313
			WO 2003-EP2515	W 20030311

OTHER SOURCE(S): MARPAT 139:261308
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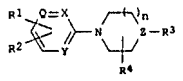

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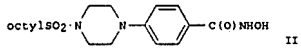


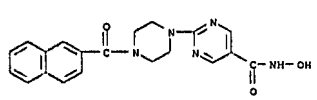
II

AB This invention comprises aryl and heteroaryl hydroxamic acids (shown as I; variables defined below; e.g. II) having histone deacetylase inhibiting enzymic activity; their preparation, compns. containing them and their use as a medicine. Compds. I show excellent in-vitro histone deacetylase inhibiting enzymic activity, have advantageous properties with regard to cellular activity and specific properties with regard to inhibition of cell cycle progression at both G1 and G2 checkpoints (p21 induction capacity), and show good metabolic stability and high bioavailability and more particular show oral bioavailability. They can also be used for detection and identification of histone deacetylase. General synthetic procedures and characterization data for twenty-seven I are

included; also, prepns. of 12 intermediates are included. For example, a 59 % yield of 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5-carbohydroxamic acid was obtained by removing the O-tetrahydropyranyl group of its ester using trifluoroacetic acid; the ester was prepared in 61 % yield from N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride, sodium 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5-carboxylate, O-(tetrahydro-2H-pyran-2-yl)hydroxylamine, and 1-hydroxy-1H-benzotriazole in CH2Cl2/THF. The sodium salt was obtained by base hydrolysis of the Et ester; the ester was prepared in 73 % yield from Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate and dimethylsulfamoyl chloride; Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate was obtained in <96 % yield from Et 2-(4-benzylpiperazin-1-yl)pyrimidine-5-carboxylate by hydrogenation using Pd/C; the benzyl derivative was obtained from 1-(phenylmethyl)piperazine, (135 mL) was added gradually to a solution of potassium carbonate (0.18 mol) and 2-(methylsulfonyl)-5-pyrimidinecarboxylic acid Et ester, K2CO3 in MeCN. For I: n is 0-3; Q, X and Y are N or C; Z is N or CH; R1 is -C(O)NR5R6, -N(H)C(O)R7, -C(O)-C1-6alkanediylSR7, -NR8C(O)N(OH)R7, -NR8C(O)C1-6alkanediylSR7, -NR8C(O)C:N(OH)R7 or another Zn-chelating-group; R2 is H, halo, hydroxy, amino, nitro, C1-6alkyl, C1-6alkyloxy, trifluoromethyl, di(C1-6-alkyl)amino, hydroxyamino or naphthalenylsulfonylpyrazinyl. R3 is H, C1-6-alkyl, arylC2-6alkenediyl, furanylcarbonyl, naphthalenylcarbonyl, -C(O)phenylR9, C1-6alkylaminocarbonyl, aminosulfonyl, arylaminosulfonyl, aminosulfonylamino, di(C1-6-alkyl)aminosulfonylamino, arylaminosulfonylamino, aminosulfonylaminoC1-6-alkyl, di(C1-6-alkyl)aminosulfonylaminoC1-6-alkyl, arylaminosulfonylaminoC1-6alkyl, di(C1-6-alkyl)aminoC1-6alkyl, C11-12-alkylsulfonyl, di(C1-6-alkyl)aminosulfonyl, trihaloC1-6-alkylsulfonyl, di(aryl)C1-6alkylcarbonyl, thiophenylC1-6alkylcarbonyl, pyridinylcarbonyl or arylC1-6alkylcarbonyl. R4 is H, hydroxy, amino, hydroxyC1-6alkyl, C1-6alkyl, C1-6alkyloxy, arylC1-6alkyl, aminocarbonyl, hydroxycarbonyl, aminoC1-6-alkyl, aminocarbonylC1-6-alkyl, hydroxycarbonylC1-6-alkyl, hydroxyaminocarbonyl, C1-6-alkyloxycarbonyl, C1-6-alkylaminoC1-6-alkyl or di(C1-6-alkyl)aminoC1-6-alkyl; when R3 and R4 are present on the same C atom, R3 and R4 together may form -C(O)-NH-CH2-NR10- wherein R10 is H or aryl; when R3 and R4 are present on adjacent C atoms, R3 and R4 together may form :CH-CH:CH-CH: ; addnl. details are given in the claims.

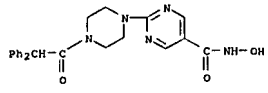
IT 603991-96-4P
RL: ARG (Analytical reagent use); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and reagent for detection/identification of histone deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-96-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylcarbonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



IT 603991-95-3P 603992-24-1P 603992-25-2P
603992-26-3P 603992-27-4P 603992-28-5P
RL: ARG (Analytical reagent use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and reagent for detection/identification of histone deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-95-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(diphenylacetyl)-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



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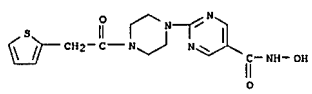

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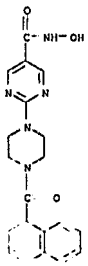
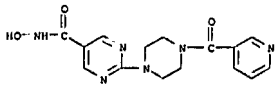


RN 603992-26-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(3-pyridinylcarbonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 603992-27-4 CAPLUS
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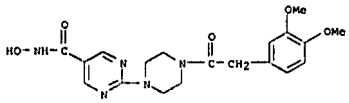
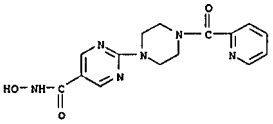
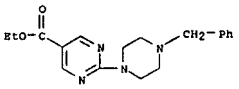


RN 603992-28-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-pyridinylcarbonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

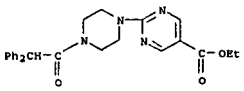


IT 603986-74-9P, Ethyl 2-(4-benzylpiperazin-1-yl)pyrimidine-5-carboxylate 603992-30-9P, Ethyl 2-[4-(diphenylacetyl)piperazin-1-yl]pyrimidine-5-carboxylate 603992-31-0P, 2-[4-(Diphenylacetyl)piperazin-1-yl]pyrimidine-5-carboxylic acid 603992-32-1P 603992-34-3P 603992-37-6P, Ethyl 2-[4-[(naphthalen-2-yl)carbonyl]piperazin-1-yl]pyrimidine-5-carboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

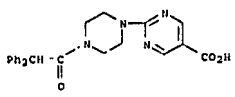
RN 603986-74-9 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-(phenylmethyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 603992-30-9 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-(diphenylacetyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 603992-31-0 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-(diphenylacetyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 603992-32-1 CAPLUS
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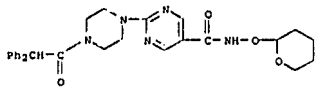
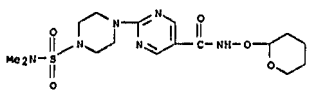
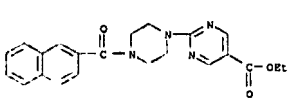


RN 603992-34-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(dimethylamino)sulfonyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



RN 603992-37-6 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 2-[4-(2-naphthalenylcarbonyl)-1-piperazinyl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:669444 CAPLUS
DOCUMENT NUMBER: 140:70519
TITLE: Histone Deacetylase Inhibitor LAQ824 Both Lowers Expression and Promotes Proteasomal Degradation of Bcr-Abl and Induces Apoptosis of Imatinib Mesylate-sensitive or -refractory Chronic Myelogenous Leukemia-Blast Crisis Cells
AUTHOR(S): Nimmanapalli, Ramadevi; Puino, Lianne; Bali, Purva; Gasparetto, Maura; Glozak, Michele; Tao, Jianguo; Moscinski, Lynn; Smith, Clayton; Wu, Jie; Jove, Richard; Atadja, Peter; Bhalla, Kapil
CORPORATE SOURCE: Department of Interdisciplinary Oncology, Moffitt Cancer Center and Research Institute University of South Florida, Tampa, FL, USA
SOURCE: Cancer Research (2003), 63(16), 5126-5135
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

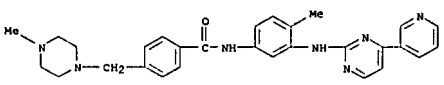
AB Treatment with LAQ824, a cinnamyl hydroxamic acid analog inhibitor of histone deacetylases, depleted the mRNA and protein expression of Bcr-Abl in human chronic myeloid leukemia blast crisis (CML-BC) cells. Exposure to LAQ824 induced the expression of the cell cycle-dependent kinase inhibitors p21 and p27 and caused cell cycle G1-phase accumulation and apoptosis of CML-BC cells. LAQ824 also induced acetylation of heat shock protein 90. This inhibited the chaperone association of Bcr-Abl with heat shock protein 90, thereby promoting the proteasomal degradation of Bcr-Abl. Cotreatment with LAQ824 increased imatinib mesylate-induced apoptosis of CML-BC cells. Addnl., LAQ824 down-regulated the levels of mutant Bcr-Abl possessing the T315I point mutation, as well as induced apoptosis of imatinib-refractory primary CML-BC cells. Therefore, LAQ824 may be a promising therapeutic agent in the treatment of imatinib-sensitive or -refractory human leukemia.

IT 220127-57-1, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitor LAQ824 induces apoptosis of imatinib mesylate-sensitive or -refractory chronic myelogenous leukemia-blast crisis cells)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



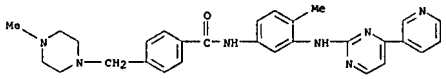
CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:638789 CAPLUS
DOCUMENT NUMBER: 139:228345
TITLE: An activated receptor tyrosine kinase, TEL/PDGFβR, cooperates with AML1/ETO to induce acute myeloid leukemia in mice
AUTHOR(S): Grisolano, Jay L.; O'Neal, Julie; Cain, Jennifer; Tomasson, Michael H.
CORPORATE SOURCE: Departments of Medicine and Genetics, Division of Oncology, Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(16), 9506-9511
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The t(8;21)(q22;q22) translocation, occurring in 40% of patients with acute myeloid leukemia (AML) of the FAB-M2 subtype (AML with maturation), results in expression of the RUNX1-CBF2T1 [AML1-ETO (AE)] fusion oncogene. AML/ETO may contribute to leukemogenesis by interacting with nuclear core-pressor complexes that include histone deacetylases , which mediate the repression of target genes. However, expression of AE is not sufficient to transform primary hematopoietic cells or cause disease in animals, suggesting that addnl. mutations are required. Activating mutations in receptor tyrosine kinases (RTK) are present in at least 30% of patients with AML. To test the hypothesis that activating RTK mutations cooperate with AE to cause leukemia, we transplanted retrovirally transduced murine bone marrow coexpressing TEL-PDGFRB and AE into lethally irradiated syngeneic mice. These mice (19/19, 100%) developed AML resembling M2-AML that was transplantable in secondary recipients. In contrast, control mice coexpressing with TEL-PDGFRB and a DNA-binding-mutant of AE developed a non-transplantable myeloproliferative disease identical to that induced by TEL-PDGFRB alone. We used this unique model of AML to test the efficacy of pharmacol. inhibition of histone deacetylase activity by using trichostatin A and suberoy-lanilide hydroxamic acid alone or in combination with the tyrosine kinase inhibitor, imatinib mesylate. We found that although imatinib prolonged the survival of treated mice, histone deacetylase inhibitors provided no addnl. survival benefit. These data demonstrate that an activated RTK can cooperate with AE to cause AML in mice, and that this system can be used to evaluate novel therapeutic strategies.
IT 152459-95-5, Imatinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(although imatinib prolonged the survival of treated mice, histone deacetylase inhibitors provided no addnl.

survival benefit)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



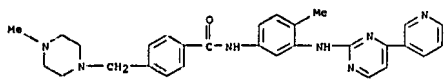
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:335539 CAPLUS
DOCUMENT NUMBER: 139:190814
TITLE: Histone Deacetylase Inhibitors Promote STI571-mediated Apoptosis in STI571-sensitive and -resistant Bcr/Abl+ Human Myeloid Leukemia Cells
AUTHOR(S): Yu, Chunrong; Rahmani, Mohamed; Almenara, Jorge; Subler, Mark; Krystal, Geoffrey; Conrad, Daniel; Varticovski, Lubya; Dent, Paul; Grant, Steven
CORPORATE SOURCE: Department of Medicine, Virginia Commonwealth University, Medical College of Virginia, Richmond, VA, 23298, USA
SOURCE: Cancer Research (2003), 63(9), 2118-2126
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interactions between the Bcr/Abl kinase inhibitor STI571 (Gleevec, imatinib mesylate) and histone deacetylase inhibitors (HDIs) have been examined in STI571-sensitive and -resistant Bcr/Abl+ human leukemia cells (K562 and LAMA 84). Cotreatment of K562 cells with 250 nM imatinib mesylate and 2.0 μM suberoylanilide hydroxamic acid (SAHA) for 24 h, exposures that were minimally toxic alone, resulted in a marked increase in mitochondrial damage (e.g., cytochrome c, Smac/DIABLO, and apoptosis-inducing factor release), caspase activation, and apoptosis. Similar events were observed in other Bcr/Abl+ cells (i.e., LAMA 84), and in cells exposed to STI571 in combination with the HDI sodium butyrate. Coexposure of cells to HDIs in conjunction with STI571 resulted in multiple perturbations in signaling and cell cycle-regulatory proteins, including down-regulation of Raf, phospho-mitogen-activated protein kinase kinase (MEK), phospho-extracellular signal-regulated kinase (ERK), phospho-Akt, phospho-signal transducers and activators of transcription 5, cyclin D1, and Mcl-1, accompanied by dephosphorylation and cleavage of retinoblastoma protein and a striking increase in phosphorylation of c-Jun NH2-terminal kinase. Coexposure of Bcr/Abl+ cells to STI571 also blocked SAHA-mediated induction of p21CIP1 and resulted in down-regulation of Bcr/Abl protein expression. STI571 and SAHA also interacted synergistically to induce apoptosis in STI571-resistant K562 and LAMA 84 cells that display increased Bcr/Abl protein expression. Lastly, inducible expression of a constitutively active MEK1/2 construct significantly attenuated SAHA/STI571-mediated apoptosis in K562 cells, implicating disruption of the Raf/MEK/ERK axis in synergistic antileukemic

effects of this drug combination. Together, these findings indicate that combined exposure of Bcr/Abl+ cells to the kinase inhibitor STI571 and HDIs leads to diverse perturbations in signaling and cell cycle-regulatory proteins, associated with a marked increase in mitochondrial damage and cell death. They also raise the possibility that this strategy may be effective in some Bcr/Abl+ cells that are resistant to STI571 through increased Bcr/Abl expression.
IT 220127-57-1, STI571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leukemia cell apoptosis induced by STI571 and histone deacetylase inhibitor combination via perturbations in expression of signaling, cell cycle-, and apoptosis-regulatory proteins)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



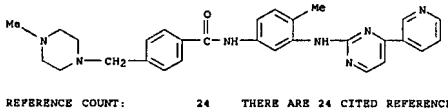
CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:314976 CAPLUS
DOCUMENT NUMBER: 139:159591
TITLE: Cotreatment with the histone deacetylase inhibitor suberoylanilide hydroxamic acid (SAHA) enhances imatinib-induced apoptosis of Bcr-Abl-positive human acute leukemia cells
AUTHOR(S): Nimmanapalli, Ramadevi; Fuino, Lianne; Stobaugh,

Corinne; Richon, Victoria; Bhalla, Kapil
CORPORATE SOURCE: Department of Interdisciplinary Oncology, Moffitt Cancer Center and Research Institute, University of South Florida, Tampa, USA
SOURCE: Blood (2003), 101(8), 3236-3239
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Here we demonstrate that treatment with SAHA (suberoylanilide hydroxamic acid), a known inhibitor of histone deacetylases (HDACs), alone induced p21 and/or p27 expressions but decreased the mRNA and protein levels of Bcr-Abl, which was associated with apoptosis of Bcr-Abl-expressing K562 and LAMA-84 cells. Co-treatment with SAHA and imatinib (Gleevec) caused more down-regulation of the levels and auto-tyrosine phosphorylation of Bcr-Abl and apoptosis of these cell types, as compared with treatment with either agent alone ($P < .05$). This finding was also associated with a greater decline in the levels of phospho-AKT and Bcl-xL. Significantly, treatment with SAHA also down-regulated Bcr-Abl levels and induced apoptosis of CD34+ leukemia blast progenitor cells derived from patients who had developed progressive blast crisis (BC) of chronic myelocytic leukemia (CML) while receiving therapy with imatinib. Taken together, these findings indicate that cotreatment with SAHA enhances the cytotoxic effects of imatinib and may have activity against imatinib-refractory CML-BC.
IT 152459-95-5, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cotreatment with the histone deacetylase inhibitor suberoylanilide hydroxamic acid (SAHA) enhances imatinib-induced apoptosis of Bcr-Abl-pos. human acute leukemia cells)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:43028 CAPLUS
DOCUMENT NUMBER: 138:106596
TITLE: Preparation of thiophenedicarboxamides and related compounds as histone deacetylase (HDAC) inhibitors.
INVENTOR(S): Leser-Reiff, Ulrike; Sattelkau, Tim; Zimmermann, Gerd
PATENT ASSIGNEE(S): Hoffman-LA Roche, Inc., Germany
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003013757	A1	20030116	US 2002-167677	20020611 <--
US 6794173	B2	20040831		
CA 2449804	A1	20030213	CA 2002-2449804	20020613 <--
WO 2003011851	A2	20030213	WO 2002-EP6488	20020613 <--
WO 2003011851	A3	20030918		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002355626	A1	20030217	AU 2002-355626	20020613 <--
EP 1401824	A2	20040331	EP 2002-791436	20020613
EP 1401824	B1	20061025		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
CN 1516697	A	20040728	CN 2002-812010	20020613
BR 2002010424	A	20040817	BR 2002-10424	20020613
NZ 529874	A	20041224	NZ 2002-529874	20020613
JP 2005502641	T	20050127	JP 2003-517043	20020613
AT 341569	T	20061115	AT 2002-791436	20020613
RU 2289580	C2	20061220	RU 2003-137578	20020613
ZA 2003009260	A	20050228	ZA 2003-9260	20031127
IN 2003CN01981	A	20060106	IN 2003-CN1981	20031211
BG 108450	A	20050131	BG 2003-108450	20031215
US 2004214862	A1	20041028	US 2004-847166	20040517
HK 1065787	A1	20061117	HK 2004-108497	20041029
PRIORITY APPLN. INFO.:			EP 2001-114496 A	20010615
			US 2002-167677 A3	20020611
			WO 2002-EP6488 W	20020613

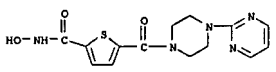
OTHER SOURCE(S): MARPAT 138:106596

AB HONHCOACONR1R2 [A = (substituted) Ph, thienyl; R1, R2 = H, (substituted) alkyl, carbocyclyl, heterocyclyl; NR1R2 = (substituted) 3-6 membered ring], were prepared Thus, thiophene-2,5-dicarboxylic acid monomethyl ester and N-methylmorpholine in CH2Cl2 at -10° were treated with 1-aminomethylnaphthalene in CH2Cl2; the mixture was stirred 90 min to give 58% monoamide. This was stirred with NH2OH.HCl and NaOMe in MeOH for 4 h to give thiophene-2,5-dicarboxylic acid 2-hydroxyamide 5-[(naphthalen-1-ylmethyl)amide]. Tested title compds. inhibited HT-29 tumor cell growth with IC50 = 0.02-0.17 μM. A tablet formulation is given.

IT 487004-17-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of thiophenedicarboxamides and related compds.
as histone deacetylase (HDAC) inhibitors)

RN 487004-17-1 CAPLUS
CN 2-Thiophenecarboxamide, N-hydroxy-5-[[4-(2-pyrimidinyl)-1-

piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

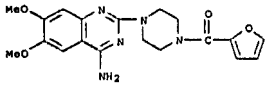
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103 <--
WO 2001032928	A3	20020725		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
PRIORITY APPLN. INFO.:			US 1999-165398P P	19991105
			US 2000-196571P P	20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and

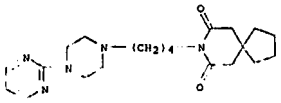
apparatus useful for identifying hypersensitivity in a subject are also disclosed.

IT 19216-56-9, Prazosin 36505-84-7, Buspirone 63590-64-7, Terazosin 74191-85-8, Doxazosin 171599-83-0, Sildenafil citrate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods of determining individual hypersensitivity to a pharmaceutical agent
from gene expression profile)

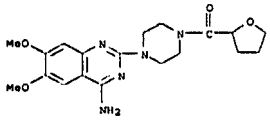
RN 19216-56-9 CAPLUS
CN Methanone, [4-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl]-2-furanyl- (CA INDEX NAME)



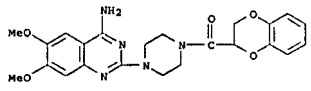
RN 36505-84-7 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]- (CA INDEX NAME)



RN 63590-64-7 CAPLUS
CN Methanone, [4-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl](tetrahydro-2-furanyl)- (CA INDEX NAME)



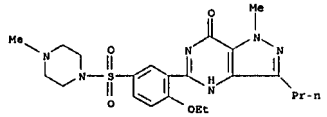
RN 74191-85-8 CAPLUS
CN Methanone, [4-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl](2,3-dihydro-1,4-benzodioxin-2-yl)- (CA INDEX NAME)



RN 171599-83-0 CAPLUS
CN 7H-Pyrazolo[4,3-d]pyrimidin-7-one, 5-[2-ethoxy-5-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-1,6-dihydro-1-methyl-3-propyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (CA INDEX NAME)

CM 1

CRN 139755-83-2
CMF C22 H30 N6 O4 S



CM 2

CRN 77-92-9
CMF C6 H8 O7